DEPARTMENT OF HEALTH & HUMAN SERVICES

P05

Public Health Service

Memorandum

P920046

Date SEP - 5 1996

From Director, Office of Device Evaluation (HFZ-400)
Center for Devices and Radiological Health (CDRH)

Subject Premarket Approval of Femcare Ltd.
Filshie Clip System™ (Mark VI) - ACTION

To The Director, CDRH
ORA _____

ISSUE. Publication of a notice announcing approval of the subject PMA.

FACTS. Tab A contains a FEDERAL REGISTER notice announcing:

(1) a premarket approval order for the above referenced medical device (Tab B); and

(2) the availability of a summary of safety and effectiveness data for the device (Tab C).

RECOMMENDATION. I recommend that the notice be signed and published.

Susan Alpert, Ph.D., M.D.

Attachments
Tab A - Notice
Tab B - Order
Tab C - S & E Summary

DECISION

Approved _____ Disapproved _____ Date _____

Prepared by Donna-Bea Tillman, Ph.D. CDRH, HFZ-470, 7/29/96, 594-1180

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

DRAFT

[DOCKET NO. _____]

Femcare Ltd.™; Premarket Approval of Filshie Clip System™ Mark VI

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing its approval of the application submitted by Family Health International, Research Triangle Park, NC, U.S. Representative for Femcare™ Ltd., Nottingham, U.K., for premarket approval, under the Federal Food, Drug, and Cosmetic Act (the act), of the Filshie Clip System™ (Mark VI). After reviewing the recommendation of the Obstetrics and Gynecology Devices Panel, FDA's Center for Devices and Radiological Health (CDRH) notified the applicant, by letter on September 5, 1996, of the approval of the application.

DATES: Petitions for administrative review by (insert date 30 days after date of publication in the FEDERAL REGISTER).

ADDRESSES: Written requests for copies of the summary of safety and effectiveness data and petitions for administrative review, to the Dockets Management Branch (HFA-305), Food and Drug Administration, 12420 Parklawn Dr., Rm. 1-23, Rockville, MD 20857.

9

FOR FURTHER INFORMATION CONTACT:

Colin M. Pollard,

Center for Devices and Radiological Health (HFZ-470),

Food and Drug Administration,

9200 Corporate Blvd.,

Rockville, MD 20850,

301-594-1180.

SUPPLEMENTARY INFORMATION: On September 10, 1993, Family Health International, Research Triangle Park, NC, U.S. Representative for Femcare Ltd.™ Nottingham, NG73, England, submitted to CDRH an application for premarket approval of the Filshie Clip System™ (Mark VI). The device is a contraceptive tubal occlusion device (TOD) indicated for permanent female sterilization by occlusion of the fallopian tubes.

On February 26, 1996, the Obstetrics and Gynecology Devices Panel, an FDA advisory committee, reviewed and recommended approval of the application.

On September 5, 1996, CDRH approved the application by a letter to the applicant from the Director of the Office of Device Evaluation, CDRH.

A summary of the safety and effectiveness data on which CDRH based its approval is on file in the Dockets Management Branch (address above) and is available from that office upon written request. Requests should be identified with the name of the device and the docket number found in brackets in the heading of this document.

39

Opportunity for Administrative Review

Section 515(d)(3) of the act, (21 U.S.C. 360e(d)(3)) authorizes any interested person to petition, under section 515(g) of the act, for administrative review of CDRH's decision to approve this application. A petitioner may request either a formal hearing under part 12 (21 CFR part 12) of FDA's administrative practices and procedures regulations or a review of the application and CDRH's action by an independent advisory committee of experts. A petition is to be in the form of a petition for reconsideration under 10.33(b) (21 CFR 10.33(b)). A petitioner shall identify the form of review requested (hearing or independent advisory committee) and shall submit with the petition supporting data and information showing that there is a genuine and substantial issue of material fact for resolution through administrative review. After reviewing the petition, FDA will decide whether to grant or deny the petition and will publish a notice of its decision in the FEDERAL REGISTER. If FDA grants the petition, the notice will state the issue to be reviewed, the form of the review to be used, the persons who may participate in the review, the time and place where the review will occur, and other details.

Petitioners may, at any time on or before (insert date 30 days after date of publication in the FEDERAL REGISTER), file with the Dockets Management Branch (address above) two copies of each petition and supporting data and information, identified with the name of the device and the docket number found in brackets in the heading of this document. Received petitions may be seen in the office above between 9 a.m. and 4 p.m., Monday through Friday.

This notice is issued under the Federal Food, Drug, and Cosmetic Act (secs. 515(d), 520(h), (21 U.S.C. 360e(d), 360j(h))) and under authority delegated to the Commissioner of Food and Drugs (21 CFR 5.10) and redelegated to the Director, Center for Devices and Radiological Health (21 CFR 5.53).

Dated:_____.

_____

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850

Femcare Ltd.
Ms. Julie Omohundro
Associate Director
Regulatory Affairs and
Quality Assurance
Family Health International
P.O. Box 13950
Research Triangle Park, North Carolina 27709

SEP - 5 1996

Re: P920046
Filshie Clip System™ (Mark VI)
Filed: September 10, 1992
Amended: October 14, 1992, March 17, April 23 and 27, June 3, August 20 and 30, and December 2, 1993; January 3, 11 and 14, February 18, April 25, May 26, August 3 and 30, October 13, November 21, December 1 and 27, 1994; January 4, February 24, June 27, August 21, September 1, October 31, November 13, December 4, 12, and 29, 1995; June 12, and August 14, 1996

Dear Ms. Omohundro:

The Center for Devices and Radiological Health(CDRH)of the Food and Drug Administration (FDA) has completed its review of your premarket approval application (PMA) for the Filshie Clip System™ (Mark VI). The device is a contraceptive tubal occlusion device (TOD) indicated for permanent female sterilization by occlusion of the fallopian tubes. We are pleased to inform you that the PMA is approved subject to the conditions described below and in the "Conditions of Approval" (enclosed). You may begin commercial distribution of the device upon receipt of this letter.

The sale, distribution, and use of this device are restricted to prescription use in accordance with 21 CFR 801.109 within the meaning of section 520(e) of the Federal Food, Drug and Cosmetic Act (the act) under the authority of section 515(d)(1)(B)(ii) of the act. FDA has also determined that to ensure the safe and effective use of the device that the device is further restricted within the meaning of section 520(e) under the authority of section 515(d)(1)(B)(ii), (1) insofar as the labeling specify the requirements that apply to the training of practioners who may use the device as approved in this order and (2) insofar as the sale, distribution, and use must not violate sections 502(q) and (r) of the act.

Expiration dating for this device has been established and approved at 6 months. This is to advise you that the protocol you used to establish this expiration dating is considered an approved protocol for the purpose of extending the expiration dating as provided by 21 CFR 814.39(a)(8).

CDRH will publish a notice of its decision to approve your PMA in the FEDERAL REGISTER. The notice will state that a summary of the safety and effectiveness data upon which the approval is based is available to the public upon request. Within 30 days of publication of the notice of approval in the FEDERAL REGISTER, any interested person may seek review of this decision by requesting an

9

opportunity for administrative review, either through a hearing or review by an independent advisory committee, under section 515(g) of the Federal Food, Drug, and Cosmetic Act (the act).

Failure to comply with the conditions of approval invalidates this approval order. Commercial distribution of a device that is not in compliance with these conditions is a violation of the act.

You are reminded that, as soon as possible and before commercial distribution of your device, you must submit an amendment to this PMA submission with copies of all approved labeling in final printed form.

All required documents should be submitted in triplicate, unless otherwise specified, to the address below and should reference the above PMA number to facilitate processing.

PMA Document Mail Center (HFZ-401)
Center for Devices and Radiological Health
Food and Drug Administration
9200 Corporate Blvd.
Rockville, Maryland 20850

If you have any questions concerning this approval order, please contact Mr. Colin M. Pollard at (301) 594-1180.

Sincerely yours,

Susan Alpert, Ph.D., M.D.
Director
Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosure

8

SUMMARY OF SAFETY AND EFFECTIVENESS

I. GENERAL INFORMATION

Device Generic Name: Contraceptive Tubal Occlusion Device (TOD) and Introducer

Device Trade Name: Filshie Clip System™ (Mark VI)

Applicant's Name and Address:

Femcare™ Ltd
St. Peters St.
Nottingham NG7 3EN
United Kingdom

U.S. Representative

Julie Omohundro
Associate Director, Regulatory
Affairs and Quality Assurance
Family Health International
P.O. Box 13950
Research Triangle Park,
North Carolina 27709

Premarket Approval Application (PMA) Number: P920046

Date of Panel Recommendation: February 26, 1996

Date of Notice of Approval to Applicant: SEP - 5 1996

II. INDICATION FOR USE

The Filshie Clip System™ (Mark VI) is indicated for permanent female sterilization by occlusion of the fallopian tubes.

III. DEVICE DESCRIPTION

The Filshie Clip System™ (Mark VI) (hereinafter called the Filshie Clip) consists of a pair of permanently implantable clips and a series of applicators that are used to apply the clip to the Fallopian tubes.

The Filshie Clip

The Filshie Clip consists of a rigid titanium body and a cross-linked silicone rubber lining. The upper and lower jaws are joined at one end by a hinge. Attached to the open end of the upper jaw of the Clip is a small 'no-touch' handle that is used to load the Clip into the applicator and then is detached from the Clip.

4

The Filshie Clip Applicators

Several applicators are available for use with the Filshie Clip System™. One is designed for use with minilaparotomy, and the rest are designed to be used during various laparoscopic techniques. All parts of the applicator which come into contact with the patient are made of stainless steel.

- The FC-4 applicator is intended for minilaparotomy procedures. It is 200 mm in overall length with an effective shaft length of 100 mm.

- The FC-10A applicator is intended for single-incision laparoscopy. Designed for use with an operating laparoscope that has a working channel of 6 or 7 mm diameter, it is 5 mm in diameter and 545 mm in overall length with an effective shaft length of 440 mm.

- The FC-6A applicator is intended for single-incision laparoscopy. Designed for use with an operating laparoscope having a working channel of 8 mm diameter minimum, it is 7.8 mm in diameter and 520 mm in overall length with an effective shaft length of 415 mm.

- The FC-7A applicator is intended for dual-incision laparoscopy. Designed for use with the 7 mm internal diameter Filshie trocar and cannula, it is 7 mm in diameter and 355 mm in overall length with an effective shaft length of 250 mm.

- The FC-2A applicator is intended for dual-incision laparoscopy. Designed for use with the 8 mm internal diameter Filshie trocar and cannula, it is 8 mm in diameter and 355 mm in overall length with an effective shaft length of 250 mm.

Principles of Operation

The sterile Filshie Clip is loaded into the applicator using the 'no-touch' handle and aseptic technique. The applicator is introduced into the abdominal cavity through a cannula or laparoscope and maneuvered so that the Fallopian tube is captured transversely in the jaws of the Clip. To allow passage through the cannula or laparoscope, the jaws of the applicator must be half closed. The Clip will not latch when the jaws are in this position and, when pressure on the finger bar is released, the jaws of both applicator and Clip will re-open.

To close the Clip, the finger bar is gently squeezed until a physical stop is reached. The pressure on the finger bar transmits force along the shaft of the applicator, closing the upper jaw of the applicator and exerting pressure on the Clip. The pressure from the applicator jaws forces the upper jaw of the Clip down over the Fallopian tube. Additional pressure flattens the curved upper jaw of the Clip and pushes its tip under the lip of the lower jaw, locking the Clip into position on the Fallopian tube.

IV. CONTRAINDICATIONS, WARNINGS AND PRECAUTIONS

Use of the Filshie Clip is contraindicated in the presence of any of the following conditions:

1. pregnancy or suspicion of pregnancy
2. significant peritubular adhesions obscuring the portion of the fallopian tube to be occluded and impairing tubal mobility
3. acute pelvic inflammatory disease
4. salpingitis isthmica nodosa or chronic isthmic induration
5. hemoperitoneum or suspicion of ectopic pregnancy
6. any conditions contraindicating surgery or the use of anesthesia

The warnings and precautions can be found in the Professional Labeling (Attachment A).

V. ADVERSE EFFECTS OF THE DEVICE ON HEALTH

(See Table 1 for a listing of adverse events reported during the 10 prospective clinical studies included in the PMA).

A. Reported Adverse Effects

The following adverse effects have been reported with the use of the Filshie Clip.

pregnancy (0.46%); ectopic pregnancy (0.016%); clip migration or expulsion (0.13%); misapplication to ovarian ligament, broad ligament, omentum, bowel, tubal serosa, cornual or broad ligament (0.05%); pain and cramping (35.7%);

Other adverse effects reported from surgical procedures to implant the Filshie Clip include the following:

musculoskeletal pain (6.0%); adnexal pain/enlargement/infection (5.0%); incisional inflammation, bleeding, abscess or pain (4.4%); nausea/vomiting (4.0%); keloids (3.9%); headache (3.0%); serous discharge (2.8%); vaginitis (1.1%); urinary tract infection (1.0%); and hematoma (1.0%).

Table 1. Adverse Experiences Ever Occurring in > 0.5% of All Patients Post-Surgery

Adverse Events by Body System	Filshie Clip (N = 5454) No.	%	Other Tubal Occlusion Devices/Methods (N = 3845) No.	%
Digestive				
Nausea/vomiting	235	(4.3)	155	(4.0)
Musculoskeletal				
Back pain	32	(0.6)	23	(0.6)
Shoulder pain	295	(5.4)	212	(5.5)
Nervous/psychiatric				
Headache	164	(3.0)	89	(2.3)
Skin				
Keloid	214	(3.9)	196	(5.1)
Serous discharge	152	(2.8)	121	(3.1)
Primary incision inflammation	138	(2.5)	96	(2.5)
Wound abscess	29	(0.5)	36	(0.9)
Wound bleeding	23	(0.4)	21	(0.5)
Hematoma	55	(1.0)	35	(0.9)
Incomplete dehiscence	24	(0.4)	30	(0.8)
Incision pain	81	(1.5)	93	(2.4)
Urogenital				
Vaginitis	62	(1.1)	53	(1.4)
Vaginal abnormality	29	(0.5)	25	(0.7)
Dysplasia	32	(0.6)	17	(0.4)
Uterine abnormality	51	(0.9)	29	(0.8)
Menses (for condition not present at baseline)				
Excessive flow	379	(6.9)	209	(5.4)
Severe dysmenorrhea	144	(2.6)	57	(1.5)
Severe intermenstrual pelvic pain	35	(0.6)	16	(0.4)
Menorrhagia	37	(0.7)	7	(0.2)
Vaginal bleeding	79	(1.4)	65	(1.7)
Infection in adnexa	24	(0.4)	24	(0.6)
Tender/enlarged adnexa	143	(2.6)	139	(3.6)
Pelvic pain	1949	(35.7)	1652	(43.0)
Adnexal pain	109	(2.0)	91	(2.4)
Urinary tract infection	57	(1.0)	29	(0.8)

Note: Multiple complaints may be reported per woman.
Statistical comparisons may not be valid because data are pooled from 10 diverse studies.

12

B. Reported Side Effects

Menstrual pattern changes (amount of blood flow, duration of flow, cycle length, cycle regularity, and pain) may result from any sterilization procedure. Such changes occurred in 12.3% of the study subjects who received the Filshie Clip.

C. Potential Side Effects

Intraoperative and postoperative complications, in the form of major unintended surgery, febrile morbidity and rehospitalization, may occur following laparoscopic tubal sterilization. Trauma and bleeding of the pelvic organs may occur during laparoscopic Filshie Clip procedures and could result in major unplanned surgery (e.g., laparotomy).

Section VIII, Part B, of this summary discusses in greater detail the adverse effects associated with use of the Filshie Clip.

VI. ALTERNATE PRACTICES AND PROCEDURES

Alternative permanent female sterilization methods include hysterectomy, surgical resection of the fallopian tubes, ligation or fulguration (cauterization) of the fallopian tubes, and application of tubal rings (bands) or clamping devices (clips) to the fallopian tubes using other legally marketed devices.

VII. MARKETING HISTORY

The Filshie Clip System™ became commercially available in November 1982. In 1983, it was introduced in Australia, Belgium, Canada, Denmark, France, Holland, Indonesia, Italy, Malaysia, New Zealand, South Africa, Switzerland, the United Kingdom, and other countries. In 1984, it was introduced in Hong Kong and, in 1985, in Finland, Singapore, and Sweden. The Filshie Clip System™ is currently available in over 21 countries, and over 5,000 applicators and 2 million pairs of Clips have been sold worldwide. The Filshie Clip System™ has not been withdrawn from marketing for any reason relating to the safety and effectiveness of the device.

VIII. SUMMARY OF STUDIES

A. Preclinical Studies

1. Mechanical and Physical Properties

The following testing was conducted to demonstrate the mechanical and physical properties of the Filshie Clip and the applicators:

Pressure Exerted by Closed Clip

The pressure exerted by a closed clip on the fallopian tube must be known to calibrate the applicators. To determine this pressure, a clip was closed over a length of thin-walled silicone tubing connected to a controlled air supply. The entire piece of tubing was immersed in water, and the air pressure was gradually increased until a bubble began to form at the distal end of the tubing. The results demonstrated that a closed clip height of 3.8 to 4.0 mm is sufficient to withstand a pressure of 15 - 30 pounds per square inch (psi), which is at least twice normal systolic blood pressure.

Stress and Wear

Stress and wear testing was conducted to show that repeated cycling of the clips between the open and closed positions does not deform the upper jaw or cause the silicone/titanium bond to break down.

Effects of Gamma Radiation

The effects of gamma radiation on the silicone elastomer of a clip were studied using spectroscopy before and after sterilization by gamma irradiation. The results demonstrated no degradation in the silicone elastomer due to gamma irradiation.

Side-ways Pressure Force Test

The sideways pressure force required to cause detachment of the silicone lining was experimentally determined. This force is of sufficient magnitude (approximately 45 pounds force) that detachment is unlikely to occur under normal conditions of use.

Force Required to Dislodge Clip from Applicator

The force required to dislodge a clip from the applicator depends primarily on the angle of application of the force. For horizontal forces (e.g., side-loading), a force much larger than that likely to be encountered during clinical use is required to dislodge a clip. Forces oriented along the shaft of the applicator and impacts to the top of the shaft will more easily dislodge the clip.

Long-term Explantation

Mechanical testing was conducted on 43 clips that had been implanted from 5 to 196 months (median: 42 months), and 20 control clips. Testing included macroscopic visual examination, surface characteristics of the titanium, force required to open a locked clip,

and microscopic examination of the surface. The results demonstrated no significant differences between the control clips and the explanted clips. Testing to compare the chemical composition demonstrated no long-term differences between the control clips and the explanted clips.

Magnetic Resonance Imaging Compatibility

Femcare was asked to address the magnetic resonance imaging (MRI) compatibility of the Filshie Clip, to ensure patient safety should an MRI procedure be required after sterilization. Three areas of concern were addressed:

1. the static magnetic field that may attract the clip or produce a torque resulting in tissue trauma;
2. the switched gradient field that may induce a flow of electric current within the clip; and
3. the radio frequency field that may cause heating of the clip.

Testing to ensure compatibility with MRI was conducted using a 1.5 Tesla magnet. No clinically significant attractive or heating effects were observed at that field strength. However, the presence of the clips produces an MR artifact which will obscure imaging of local tissue.

2. Biocompatibility

The Filshie Clip is made from silicone rubber (a cross-linked adhesive) and titanium. The Clip was subjected to the following toxicological tests: in vitro cytotoxicity tissue culture; implantation (90 day, gross with histopathology); a Salmonella Ames bacterial mutagenesis test; a mammalian mutagenesis test (L5178Y mouse lymphoma test for mutants at the TK locus); Cytogenetic damage in-vivo (mouse micronucleus test); and sensitization. The test results indicate the biocompatibility of the Filshie Clip for the proposed intended use.

3. Long Term Tissue Toxicity

Two carcinogenicity studies, one in mice and one in rats, were conducted using a miniature version of the Filshie Clip. Although the silicone supplier for the Filshie Clip has changed since these test were concluded, FDA determined that the results are still pertinent, since the new silicone has comparable chemical properties to the original silicone.

Each study included a treatment group and a control group of 200 animals. The duration of the rat study was 104 weeks and the duration of the mouse study was 78 weeks. Based on a device weight-to-body-weight ratio, exposure to the device for rats was estimated to be approximately 21 times greater than that for humans, while that for the mice was estimated to be approximately 90 times greater than that for humans.

Each miniature device was clipped across a uterine horn, producing total occlusion of the distal uterus.

Under the conditions of these tests, there was no evidence of toxicological effects from the implanted clips. While neoplastic changes were noted at the implant site, they were believed to be related to the physical presence of the over sized clip and due to solid-state tumorigenesis. All of the pathologic changes that were noted could be attributed to either the natural disease progression in aging animals or to mechanical effects from the presence of the relatively large clips.

4. Shelf-Life Testing

Femcare has conducted real-time shelf-life testing to support expiration dating for the device. Testing includes both mechanical properties, package integrity, and sterility. To date the shelf-life has been validated for 6 months.

B. Clinical Studies

1. Description of Clinical Studies

The PMA included data from clinical studies at 40 different clinical sites to support the safety of the Filshie Clip, as well as its effectiveness in preventing pregnancy. A total of 9271 women were studied in ten prospective studies sponsored by Family Health International (FHI). These included seven prospective, comparative clinical trials; two prospective, non-comparative clinical trials (one of which compared two surgical approaches for applying the Filshie Clip); and one surveillance study. All studies were conducted under relatively similar protocols with nearly identical inclusion/exclusion criteria, and data were reported on standardized case forms.

All subjects had similar data collected for medical history, surgery and discharge, early follow-up (up to 30 days post-sterilization), and a first long-term follow-up visit at 6 months post-sterilization. Further follow-up varied by study; most women were scheduled to be followed up for 12 months, and the maximum specified follow-up period was 24 months. Similar statistical analyses and reports were prepared for each study. Individual safety analyses and reports were prepared for pivotal studies, and a pooled analysis for safety was done on all other studies. In addition, all prospective studies were pooled into an Overall Safety analysis.

Data from a prospective study sponsored by Femcare (the "Salzburg" study), for which only pregnancy data (and not adverse event data) are available, and which used a different protocol and inclusion criteria, were also included in the PMA. Lastly, data from a retrospective study, which attempted to evaluate women up to 60 months after sterilization, were also included.

All of the clinical data presented to support this PMA was collected at study sites outside of the United States. The applicant provided the documentation described in 21 CFR §814.15 for a PMA based solely on foreign clinical data.

2. Effectiveness - Pregnancy rates

a. Summary

Of the 5754 women who were enrolled in the eleven prospective clinical trials and who were sterilized using the Filshie Clip tubal occlusion system, 22 pregnancies were reported. There were no clinically significant differences between the pregnancy rates for women in the Filshie Clip groups and women in the Other Treatment Group (i.e., the control groups; women who were sterilized using other devices and procedures, as described in the following tables).

b. Pivotal Studies

The four largest and best-controlled clinical studies (6264, 6265, 6266, and 6267) were designated "pivotal studies". These studies were prospective, randomized, controlled clinical studies comparing the Filshie Clip to a legally marketed clip ("Other Clip", 6266 & 6267) or a legally marketed tubal ring ("Ring", 6264 & 6265). The method of application was either laparoscopy (6265 & 6267) or minilaparotomy (6264 & 6266) during the interval period. Table 2 shows an overview of the data from the four pivotal studies.

Table 2. Summary of four pivotal studies

Study	Control	Approach	N	Pregnancies (12mo / 24 mo)	Follow-up (months)	Study Countries
6264	Ring	Minilap	908	Filshie 0 Control 0	12	Panama,Peru,Kenya, Brazil, Mexico
6265	Ring	Lap	1825	Filshie 2 / 3 Control 2 / 2	12 / 24	Panama,Indonesia, Dominican Republic, Thailand,Mexico
6266	Other Clip	Minilap	878	Filshie 0 Control 1	12	Panama,Malaysia, Dominican Republic, Mexico
6267	Other Clip	Lap	1247	Filshie 1 / 2 Control 5 / 8	12 / 24	Haiti,Mexico, Venezuela, Guatemala

The data from studies 6264/6265 and 6266/6267 were pooled for the purposes of comparing the effectiveness of the Filshie Clip to the two control devices. The

pooled results are shown below in Table 3. There was no statistically significant difference in the pregnancy rates for the Filshie Clip versus either the legally marketed tubal clip or the legally marketed tubal ring. Although the lost-to-follow up rates are somewhat high, especially for the studies comparing the Filshie Clip to the legally marketed tubal clip, the sponsor provided a statistical analysis of the demographic characteristics of the treatment and control groups. The results of the analysis show that the two populations are demographically similar, so that the effect of the large number of subjects lost to follow-up would be expected to be the same for the Filshie and the control groups. Therefore, the comparison of the pregnancy rates should be unaffected by subjects lost-to-follow up.

Table 3. Gross Cumulative Life-Table Pregnancy Rates for Pivotal, Prospective Interval Studies (Pooled Laparoscopy and Minilaparotomy)

Pooled Pivotal Studies	Months of Follow-up	12-month Pregnancy Rate (Standard Error) per 100 Women	
		Filshie Clip System™	**Comparison Device**
Filshie vs. Other Clip (6267/6266)	12	**0.1 (0.1)** n=1063 % completing = 68.7%	**0.7 (0.3)** n=1062 % completing = 67%
Filshie vs. Ring (6265/6264)	12	**0.2 (0.1)** n=1378 % completing = 81.9%	**0.2 (0.1)** n=1355 % completing = 82.4%

c. Postpartum study

Study 6260 was a prospective, randomized study comparing the Filshie Clip to the Pomeroy method in postpartum women. In both cases the surgical approach was minilaparotomy. A total of 1400 women were enrolled in this 24-month study. Lost to follow-up rates at 24 months were 37.7% for the Filshie group and 40.9% for the Pomeroy group.

Table 4. Gross Cumulative Life-Table Pregnancy Rates for Non-Pivotal, Prospective Post-Partum study.

	Surgical Sterilization Method	Months of Follow-up	24-Month Pregnancy Rate (Standard Error) per 100 Women	
			Filshie Clip System™	**Comparison Method**
Filshie vs. Pomeroy Method (6260)	Minilaparotomy	24	1.7 (0.6) n=698	0.4 (0.3) n=702

There were nine reported pregnancies in the Filshie group, and two in the Pomeroy group. When the treated populations are compared, the difference in pregnancy rates is statistically significant (Table 4). It is known within the clinical community that tubal occlusion is less effective in postpartum women, due to anatomical changes that occur during pregnancy. However, it appears that mechanical devices such as clips and silastic bands may be even less effective than traditional electrosurgical methods. In fact, this issue was discussed during the Panel meetings for both the Ring and the Other Clip, and the labeling for those devices carries a warning about the potential decreased effectiveness in postpartum women. Such a warning is also included in the labeling for the Filshie Clip.

d. Other nonpivotal studies

The nonpivotal, prospective interval studies are summarized in Table 5.

3. Safety

In order to analyze safety issues, data from the 10 prospective FHI studies were pooled and summarized, including data on 5,454 women from the Filshie Clip group and 3,845 women from the Other Technique group. No statistical testing was done because of the wide variety of study methods used. Except where specifically described, no clinically significant differences were noted between the Filshie Clip group and the Other Technique group.

Table 5. Gross Cumulative Life-Table Pregnancy Rates for Non-Pivotal, Prospective Interval Studies

Non-Pivotal Studies	Surgical Sterilization Method	Months of Follow-up	Pregnancy Rate (Standard Error) per 100 Women	
			Filshie Clip System™	**Comparison Method**
Filshie vs. Secuclip[1] (6258)	Minilaparotomy	12	0.0 (NA) n=100	4.0 (2.3) n=85
Filshie vs. Electrocautery (6269)	Laparoscopy	12	0.4 (0.3) n=484	0.7 (0.4) n=471
Filshie Only (6249)	Laparoscopy & Open Laparoscopy	24	0.7 (0.4) n=1469	NA
Filshie Only (6700)	Laparoscopy & Minilaparotomy	12	0.0 (NA) n=199	NA
Filshie vs. Pomeroy Method and Ring[2] (6900)	Laparoscopy & Minilaparotomy	6	0.0 (NA) n=60	0.0 (NA) n=20 Pomeroy n=125 Ring
Salzberg[3]	Not Specified	24	0.0 (NA) n=300	NA

[1] No longer legally marketed
[2] Women were not randomized to sterilization method in this study.
[3] Non-FHI study using a different protocol

a. Ectopic Pregnancies

As with other tubal occlusion devices, the possibility of ectopic implantation must be considered in any patient becoming pregnant after sterilization using the

Filshie Clip. Data from ten clinical investigations include one ectopic pregnancy following the use of the Filshie Clip out of a total of 22 pregnancies.

The risk of ectopic pregnancy following the application of the Filshie Clip may be lower than the risk of ectopic pregnancy following bipolar electrocautery. In the nonpivotal study that compared the Filshie Clip with bipolar electrocautery (protocol 6269), two ectopic pregnancies were observed in the electrocautery group and none were observed in the Filshie group..

b. Menstrual Disturbances

Menstrual pattern changes may occur involving the amount of blood flow, duration of flow, cycle regularity and cycle length, and dysmenorrhea. Menstrual disturbances not present at baseline in women who received the Filshie Clip were reported as follows: 6.9% excessive flow; 0.7% menorrhagia; 1.4% vaginal bleeding; 2.6% severe dysmenorrhea; and 0.6% severe intermenstrual pelvic pain.

c. Operative Complications

i. Surgical Injuries

The rates of surgical injury were similar for the Filshie Clip group and the Other Technique group across all studies. In the pivotal comparative studies, the rate of tubal and/or mesosalpingeal injuries seen with the Filshie Clip was similar to that seen with the Other Clip, but lower than that observed with the Ring. The Filshie Clip had a significantly lower rate of surgical injury when applied via laparoscopy ($p = 0.01$). This difference was probably largely due to the difference in tubal and or mesosalpingeal injuries seen with the two devices (Filshie - 0.2%, Tubal Ring - 2.5%). The difference in surgical injuries was not statistically significant when applied via minilaparotomy ($p = 0.08$) where 4.0% and 6.5% tubal and/or mesosalpingeal injuries were observed for the Filshie Clip and Ring, respectively.

ii. Technical Failures / Unintended Major Surgery

The planned use of the Filshie Clip was changed to another technique or abandoned in 19 cases (0.35%) of the Filshie Clip group. A change of the planned approach, from laparoscopy to minilap or from laparoscopy or minilap to laparotomy, occurred in 16 cases (0.29%) of the Filshie Clip group. Two cases are included in both classifications, giving a total of 33 cases (0.61%) with technical failures or unintended major surgery. The two most common reasons reported for these difficulties were unexpected tubal abnormalities in 7 cases, and the presence of adhesions in 5 cases.

iii. Incision Complications

There were no differences in incisional complications between the Filshie Clip group and the Other Treatment group. At early follow-up (prior to 30 days post-sterilization) 8% of the Filshie Clip group had an incision complication. Including data from all follow-up visits, the most common incision complication was the development of a keloid (3.9% in the Filshie Clip group). Wound abscesses occurred in 0.5% of the Filshie Clip group, and hematomas occurred in 1.0% of the Filshie Clip group.

d. Postoperative Pain

Depending on the approach, from 26% to 37% of women reported pelvic pain immediately following surgery. The pain was generally mild, and only 1.6 to 1.7% of the women described the pain as severe. In the pivotal comparative studies there was no difference in postoperative pain between the Other Clip and Filshie Clip, but women in the Filshie Clip group were less likely to experience pain during recovery than women in the Ring group.

e. Clip Expulsions, Foreign Body Reactions, and Asymptomatic Migrations

Of the 5454 women who were enrolled in the ten prospective FHI clinical trials reported in this submission and who were sterilized using the Filshie Clip tubal occlusion system, eight (0.1%) women were reported to have experienced instances of clip migration, clip expulsion, or foreign body reaction. Three instances of clip expulsion (one each per urethra, vaginal cuff, and bowel) and two foreign body reactions were observed. Three instances of apparently asymptomatic migration of the clip were observed as incidental findings, but the frequency of this event is not known. In no instance was the reported event considered life-threatening; however, seven of the eight women underwent a surgical procedure for diagnosis or treatment of associated symptoms. The Other Clip has had similar expulsion events reported (Siew, 1991; Gooden et al, 1993).

IX. CONCLUSIONS DRAWN FROM STUDIES

In-vitro assays and acute and subchronic animal studies revealed no evidence of systemic toxicity, intracutaneous reactivity or intramuscular tissue response. Results of cytotoxicity and mutagenicity testing were negative. Life-time implantation studies in rats and mice, although conducted using silicone from a different source, provide no direct evidence of carcinogenic activity of the device materials. The stainless steel used in the applicator and the titanium used in the clips are not know to irritate or sensitize human tissues. Bench tests show that the clip should not migrate when exposed to an MRI field.

The clinical safety and effectiveness of the Filshie Clip System ™ was demonstrated in multi-center clinical trials. The cumulative 12-month pregnancy rates for women in the interval period ranged from 0.0 to 0.4 percent, while the cumulative 24-month pregnancy rate ranged from 0.0 to 1.0 percent. These rates are similar to those for other female sterilization devices (Peterson et al, 1996). There were no significant differences between the incidence of adverse events reported for the Filshie Clip when compared to the control devices. However, in the comparative postpartum study, the Filshie Clip was significantly less effective than the Pomeroy technique, with gross cumulative life-table pregnancy rates per 100 women at 24 months of 1.7 and 0.4, respectively.

In conclusion, the in-vitro and animal toxicity studies provide reasonable assurance that device materials are appropriate for the proposed intended use. The clinical studies provide reasonable assurance that the Filshie Clip System™ is safe and effective for its intended use.

X. PANEL RECOMMENDATIONS

The Obstetrics and Gynecology Devices Panel met February 26, 1996, to consider the safety and effectiveness of the Filshie Clip. The Panel considered data from the 11 clinical studies conducted by Family Health International, and concluded that there were sufficient data to provide reasonable assurance of the safety and effectiveness of the Filshie Clip for the stated indication. The Panel also recognized that final results from biocompatibility testing, magnetic resonance imaging compatibility testing, and chemical analysis of explanted clips were not available at that time. However, based on preliminary results from these studies, the panel recommended approval of the PMA with the condition that the approval of the device should be contingent upon the final testing results and several stated labeling changes.

XI. CDRH DECISION

CDRH concurred with the recommendation of the Obstetrics and Gynecology Devices Panel. On June 12, 1996, Family Health International submitted the final results for the biocompatibility, magnetic resonance compatibility, and long-term explant analysis, and the requested labeling changes. This information was found to adequately address the remaining deficiencies.

The applicant's manufacturing facility was inspected on October 25 and November 2, 1995, and was found to be in compliance with the Good Manufacturing Practices Regulations.

CDRH has determined that, based on the data submitted in the PMA, there is reasonable assurance that the Filshie Clip System™ is safe and effective for its intended use, and issued an approval order on SEP - 5 1996

XII. APPROVAL SPECIFICATIONS

Directions for Use: See the Labeling (Attachment A)

Hazards to Health from Use of the Device: See Indications, Contraindications, Warnings, precautions and Adverse Events in the labeling

Postapproval Requirements and Restrictions: See approval order

REFERENCES

Gooden MD, Hulka JF, Cristman GM, 1993. Spontaneous vaginal expulsion of Hulka clips, (Part 2) 81, 5:884-886.

Peterson, H.B. et al., 1996. The risk of pregnancy after tubal sterilization: Findings from the U.S. Collaborative Review of Sterilization. AM. J. Obstet. Gyn, 174:1161-70.

Siew L, 1991. Vaginal expulsion of a Hulka clip: a case report. J Reprod Med, 36, 9:695-696.

Draft (v3.0) August 30 1996

STERILIZATION USING THE FILSHIE CLIP

DRAFT PATIENT LABELLING

WHAT IS STERILIZATION?

Sterilization is a process that keeps you from having babies in the future. You should think of it as permanent.

This booklet will help you decide if this is the right choice for you. It has information about sterilization and what will happen after the operation.

Getting sterilized by blocking or sealing the Fallopian tubes is common among women who have decided not to have any more babies. This form of sterilization is done by several methods. The Filshie Clip is one of these methods. Sterilization using the Filshie Clip will be explained in this booklet. After you have read this booklet, you should discuss this procedure and other contraception options with your doctor before deciding to have the sterilization.

DECISIONS ABOUT STERILIZATION

It is important to remember that sterilization is a permanent method. Because of this you must think about sterilization very carefully if you are of childbearing age and do not want to become pregnant. It may be that another method of birth control would be better for you. What would happen if you wanted to have children again because you remarried or you lost your family in a tragedy?

There are reversible methods of contraception available to you. Examples of some of these methods are shown below.

* oral contraceptives (the pill)
* intrauterine devices (IUD) (Copper T and Progesterone T)
* barrier contraceptives such as
    a) condoms
    b) diaphragms /cervical caps
* vaginal sponges
* spermicides (creams, gels, foams etc)
* hormone shot (Depo-provera™)

* implantable contraceptives (Norplant™)
* natural family planning (rhythm method)

You should be aware that sterilization does not protect you against sexually transmitted diseases (STDs), including AIDS

If you decide that sterilization is the right thing for you, here is how it can be done.

Using Filshie Clips to block or seal the Fallopian tubes is one of the options. Your doctor will also tell you about other ways to block the Fallopian tubes and other surgical methods like hysterectomy (removing the uterus).

As with all surgical and medical procedures no guarantee of success can be given. A very small number of women sterilized with the Filshie Clip will become pregnant (1 - 4 per thousand women sterilized). This number is similar to the number who get pregnant using any other method to block the tubes.

Certain conditions must be met before you can be sterilized.

* You must be of legal age or married, depending on the law in your state.
* You must be sane.
* It must be **your** choice to be sterilized.

In some areas there may be a 30 day waiting period after you make the decision before the operation can be performed. This is to give you time to make sure you have made the right decision because sterilization is not reversible. This 30 day period may also apply to some government health care programs.

The consent of your partner to your sterilization is not usually required, but this is a major decision in your life and should be considered very carefully. You should discuss vasectomy as an alternative form of sterilization and may also wish to consider alternative forms of birth control.

YOUR DOCTORS CONCERNS

Before you make the decision to be sterilized your doctor will discuss with you (and possibly with your partner) your decision not to have babies in the future. Your doctor will also explain that there are a variety of surgical approaches to sterilization with the Filshie Clip and will tell you about each of them. These include:

- Laparoscopy: This is when the doctor fits the Filshie Clips to the Fallopian tubes through one, or sometimes two small (about a half an inch long) punctures in the abdominal wall, using special instruments. This operation can be performed using either a general or local anesthetic.
- Minilaparotomy: This is when the doctor fits the Filshie Clips to the Fallopian tubes through a single incision (usually about four inches long) in the abdominal wall. The operation is usually performed using a general anesthetic, but can be performed using a local anesthetic.
- Others: Other methods may be used if you have the sterilization procedure at the same time that another operation is being performed.

These discussions are aimed to make you fully understand the risks, benefits, alternatives and implications of sterilization. They will also make sure that you realize that sterilization is a permanent step

When you have agreed with your doctor to go ahead with the sterilization you will be asked to give your consent to the procedure in writing and then your operation will be scheduled.

You may change your mind about your decision at any time before your operation, even after you have signed the consent papers. If you have any doubts at all you should discuss them with your doctor.

If you think there may be the slightest chance of you wanting more children for any reason, you should not choose sterilization now.

WHAT IS A FILSHIE CLIP?

The Filshie Clip is a small, hinged clip made from titanium lined with silicone rubber. When it is applied to the Fallopian tube the Clip locks closed. The materials used to make the Clip are used in other medical devices, and have been shown to not cause reactions with the human body.

The Filshie Clip is 0.5 inches long, 0.14 inches wide and, when closed, 0.16 inches high (about the size of a pumpkin seed). It weighs about 1/100 of an ounce, and shows up on an X-ray.
If your physician recommends that you have an MRI (Magnetic Resonance Imaging) Procedure, you should inform him that you have had the Filshie Clip implanted.

Filshie Clips have been used since 1982 for sterilization. They have been associated with very few complications and difficulties.

WHAT HAPPENS DURING THE OPERATION

The illustrations below (Diagrams 1 and 2) show the Filshie Clip and how it is clamped over the Fallopian tube, and the anatomy of the uterus and tubes showing where the Filshie Clips are clamped over the Fallopian tubes.

Diagram 1 The Filshie Clip and its Method of Clamping.

Diagram 2. The Anatomy of the Uterus and Fallopian Tubes Showing the Positioning of the Filshie Clips.

It is common for the operation to be scheduled during or just after your menstrual period. This is to avoid trapping a fertilized egg in the Fallopian tube, which may cause a serious medical problem later.

On the day of the operation, a needle will be placed into a vein in your hand or arm. This will allow fluids to be given to you during the operation. If a general anesthetic is used you will be asleep during the operation. If a local anesthetic is used you will be awake. In either case you may be given some medication to help you relax before the anesthetic is used. The type of anesthesia used will depend on your medical history, personal choice and the advice of your doctor and/or anesthesiologist. The Filshie Clip will then be implanted using one of the following methods:

Minilaparotomy Method:
After the anesthetic has been given the doctor makes the incision in the abdomen. The incision is about four inches long and is usually made just below the bikini line. The incision exposes the necessary internal organs. The doctor then uses a special instrument, the Filshie Clip Applicator, to squeeze the Clips closed on the Fallopian tubes.

Diagram 3. The Filshie Clip Minilaparotomy Applicator.

The Clips block the tubes, preventing the sperm from being able to reach the egg to fertilize it. The Clips are then released automatically from the applicator and remain inside the body.

After the Clips have been applied, the instruments are taken out of the abdomen. The incision is then closed and stitched. After healing the scar that is left will pale after a period of time.

Laparoscopy Method:
The laparoscopic method is slightly different. After the anesthetic is given, a gas such as carbon dioxide is put into the abdomen through a

special needle that is inserted just below the belly button. The gas makes the abdomen swell, lifting the abdominal wall away from the internal organs. This reduces the risk of causing accidental damage to the organs when the laparoscope is used. The swelling of the abdomen goes away when the gas is released later in the operation.

A laparoscope is about as thick as a pencil. It shines light into the abdomen and acts like a small telescope. This allows the surgeon to see what he is doing . The puncture made by the special needle when the gas is introduced is slightly enlarged, to about half an inch, and the laparoscope is inserted into the opening. A special instrument, the Filshie Clip applicator is used to put the Filshie Clips on the tubes.

Diagram 4. A Filshie Clip Laparoscopic Applicator.

This is put into the abdomen either through the laparoscope or through a second half inch opening in the abdominal wall made just below the bikini line.

A Filshie Clip is put onto each Fallopian tube, using the applicator. The Clips are squeezed closed to block the tubes, preventing the sperm from being able to reach the egg to fertilize it. The Clips are then released automatically from the applicator and remain inside the body.

After the Clips have been applied, the instruments are taken out of the abdomen and the gas is released. It is common for each puncture to be closed with a single stitch and covered with a small sterile dressing such as a Band-Aid.

The Filshie Clips stay in your abdomen permanently. The Clips do not decay inside you and can be seen by X-ray. There have been no reports of ill effects because of the Clips remaining in the abdomen.

Diagrams 5 and 6 below illustrates the difference between the minilaparotomy and laparoscopy operations.

Diagrams 5 and 6. The Minilaparotomy and Laparoscopy Operations.

RISKS

All surgical procedures carry some risk of failure or complication. Complications associated with the Filshie Clips are rare. Serious problems like bowel injuries, bleeding, infections or complications from anesthesia happen in about one out of every thousand operations.

The most common, serious problem during surgery is internal bleeding. If this cannot be stopped using laparoscopic instruments the surgeon may have to perform a bigger operation to control the bleeding. This would mean that the doctor would have to make a larger incision to identify the site of the injury so that a repair could be made.

Other abdominal organs such as the bowel or bladder may be damaged during the procedure. This can usually be detected when it happens. Repair of the damage usually needs a bigger operation than sterilization. A second operation may occasionally be necessary if healing of the repaired damage is not satisfactory, however, this is not usually the case. If damage is not detected when it happens, it must be repaired with a second operation.

Report any fever or serious pain in your abdomen to your doctor **immediately**. Either of these could mean that you have an infection.

About 3 to 5 out of every thousand women who are sterilized with the Filshie Clip will become pregnant because the operation has failed. If you do get pregnant, you may have an ectopic pregnancy. The fertilized egg may become lodged in the Fallopian tube, causing it to rupture as the egg develops. This may cause internal bleeding. Report to your doctor

immediately if you miss a menstrual period or believe you may be pregnant.

Very occasionally a blood vessel that is out of place or adhesions may be found at the time of surgery. Adhesions are scar tissue that attaches the Fallopian tube to other abdominal organs making it impossible to apply the Clip properly. Either of these may require a bigger operation to complete the procedure safely. This may mean you would have to stay longer in the hospital.

There are other risks such as blood clots and even death but these are as rare as with any other relatively simple operations.

BENEFITS

There are several benefits of sterilization which make it a popular choice.

* It is permanent which means alternative birth control is no longer required.
* It is more effective than some methods of contraception.
* It gives you freedom from the fear and risks associated with an unwanted pregnancy.
* Hormone production, menstruation and sexual activity are generally not affected.

Important!

You should be aware that sterilization does not protect you against sexually transmitted diseases (STDs), including AIDs.

AFTER EFFECTS

Most women can go home about 4 hours after the operation. After the

operation you may have some after effects such as

* mild nausea
* pain in the neck or at the point of the shoulder. This is from the gas put into the abdomen.
* pain at the puncture sites on the abdomen.

These will usually disappear in one or two days and are not permanent.

You may also suffer some other minor discomforts. These are not permanent and should disappear in a few days after the operation. These may include

* a sore throat if a general anesthetic is used
* a cramping feeling and a possible feeling of weakness. These are like the discomforts some women have just before and during their menstrual period and usually disappear in a few hours.
* a discharge like a menstrual period for a day or two.
* tiredness and aching.
* a swollen feeling in the abdomen. This is because the muscles stay relaxed for a time after being stretched by the gas put into the abdomen.

The site of the puncture where the operation was performed should be kept dry for about four days to make sure it heals well. Any bruising around the puncture site should fade and disappear in about a week.

If the puncture site appears infected or is tender after a week you should contact your doctor who will examine you to make sure you have not got an infection.

After the puncture site has healed, you will have a very small scar.

Remember: Report any unusual signs or symptoms to your doctor.

If you have any remaining questions or doubts about sterilization with the Filshie Clip you should discuss them with your doctor. It is important that

you understand and are happy about everything before the operation is performed.

Pregnancy Rates for Birth Control Methods

Each value given is an estimate of the percent of women likely to become pregnant while using a particular contraceptive method for one year. These estimates are based on a variety of studies.

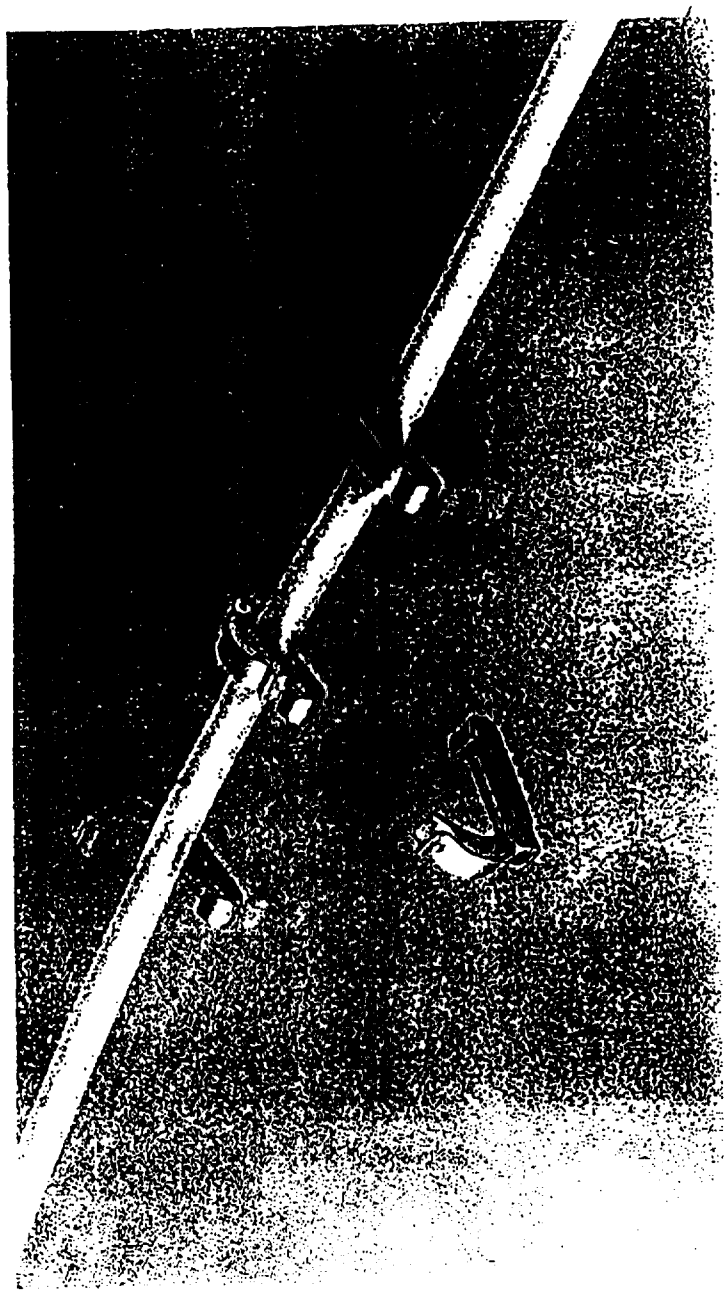
"Lowest Expected" rates indicate that the method was used correctly with every act of sexual intercourse but failed anyway (e.g., remembered to take daily hormonal contraceptive pill, but became pregnant).

"Typical" rates indicate that the method either was used incorrectly, was not used with every act of sexual intercourse, or failed during use (e.g., forgot to take daily hormonal contraceptive pill, and became pregnant).

Method	Lowest Expected	Typical
Sterilization:		
Male Sterilization	0.1%	0.15%
Female Sterilization	0.4%	0.4%
Hormonal Methods:		
Implant *(Norplant™)*	0.09%	0.09%
Hormone Shot *(Depo-Provera)*	0.3%	0.3%
Combined Pill *(Estrogen/Progestin)*	0.1%	3%
Minipill *(Progestin only)*	0.5%	3%
IUDs:		
Copper T	0.6%	0.8%
Progesterone T	1.5%	2%
Barrier Methods:		
Male Latex Condom	3%	12%
Diaphragm	6%	18%
Cervical Cap *(no previous births)*	9%	18%
Cervical Cap *(previous births)*	26%	36%
Vaginal Sponge *(no previous births)*	9%	18%
Vaginal Sponge *(previous births)*	20%	36%
Female Condom	5%	21%
Spermicide *(gel, foam, film)*	6%	21%
Natural Methods:		
Withdrawal	4%	19%
Natural Family Planning *(calendar, temperature, cervical mucus)*	1-9%	20%
No Method:	85%	85%

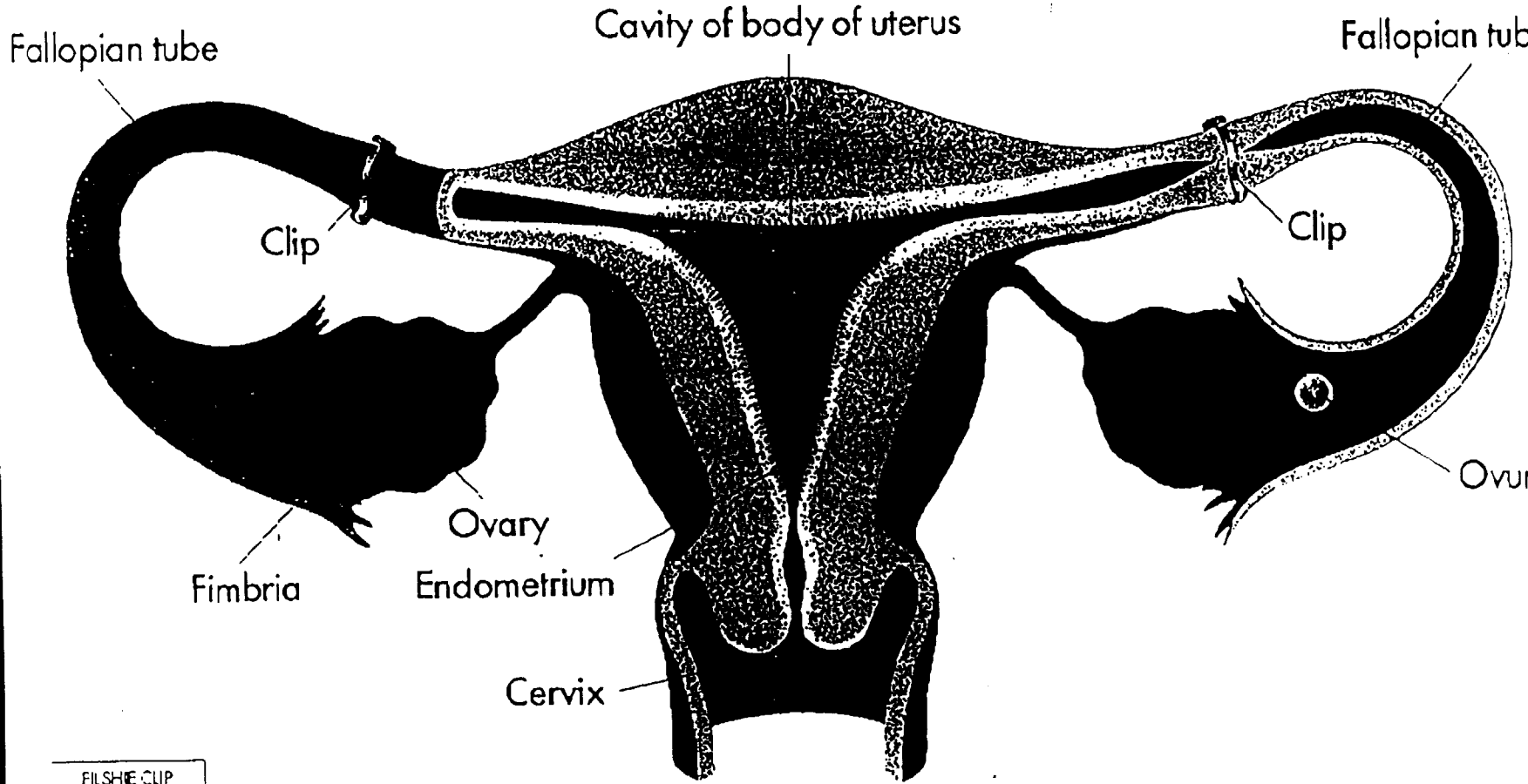
Data adapted from: R.A. Hatcher, J. Trussell, F. Stewart, et al. (eds.), Contraceptive Technology, 16th Revised edition, New York, NY: Irvington Publishers Inc., Chapter 5 (1994).

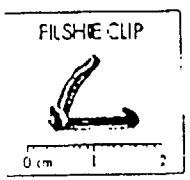
Fig 1



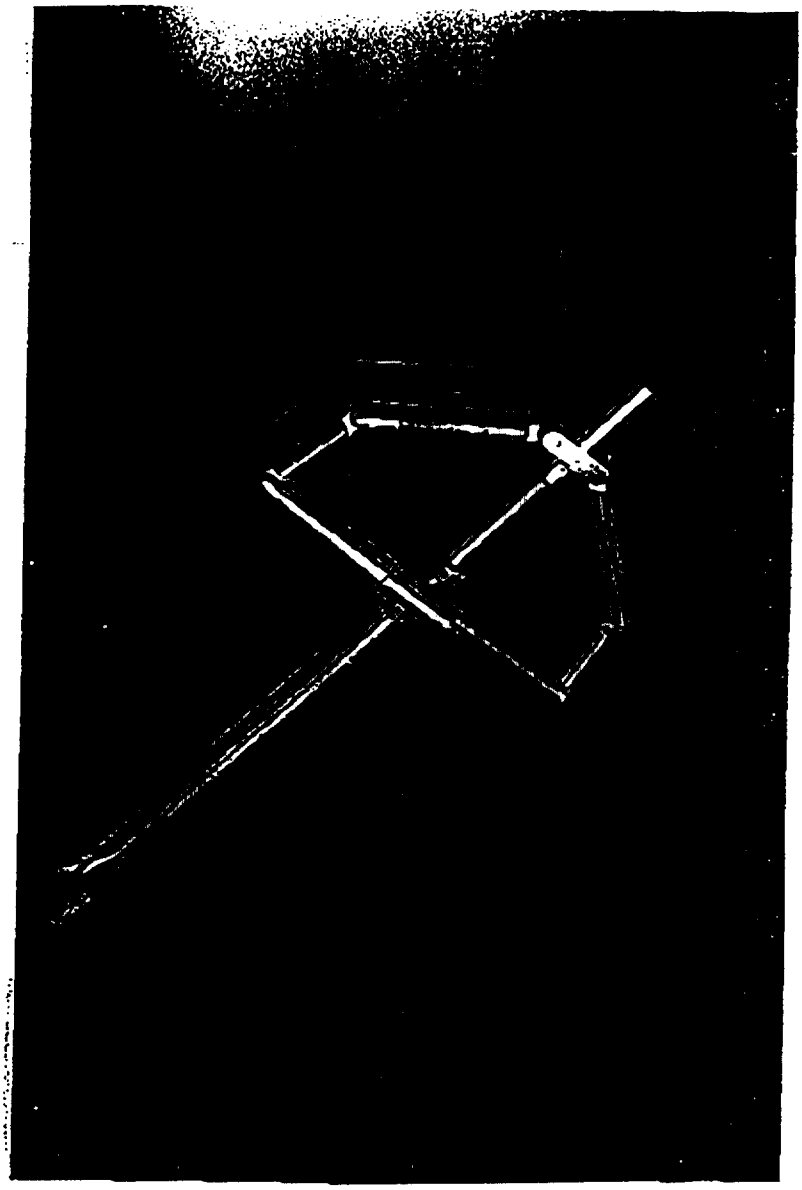
Dig 2

Female sterilisation





Diag 1.



Diag 4

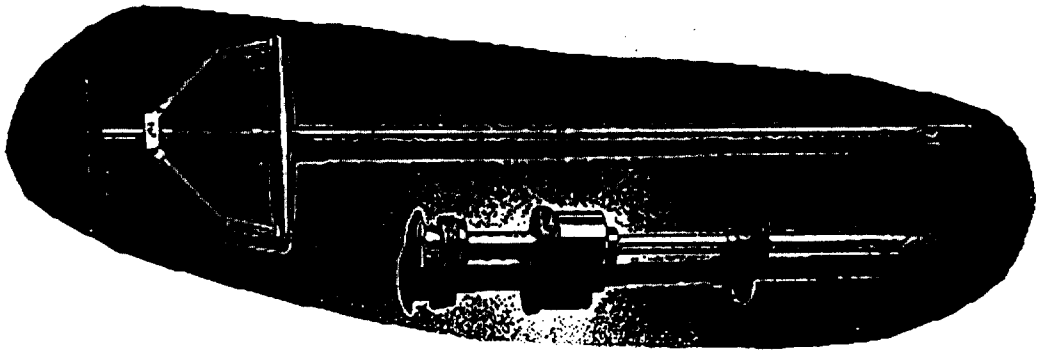
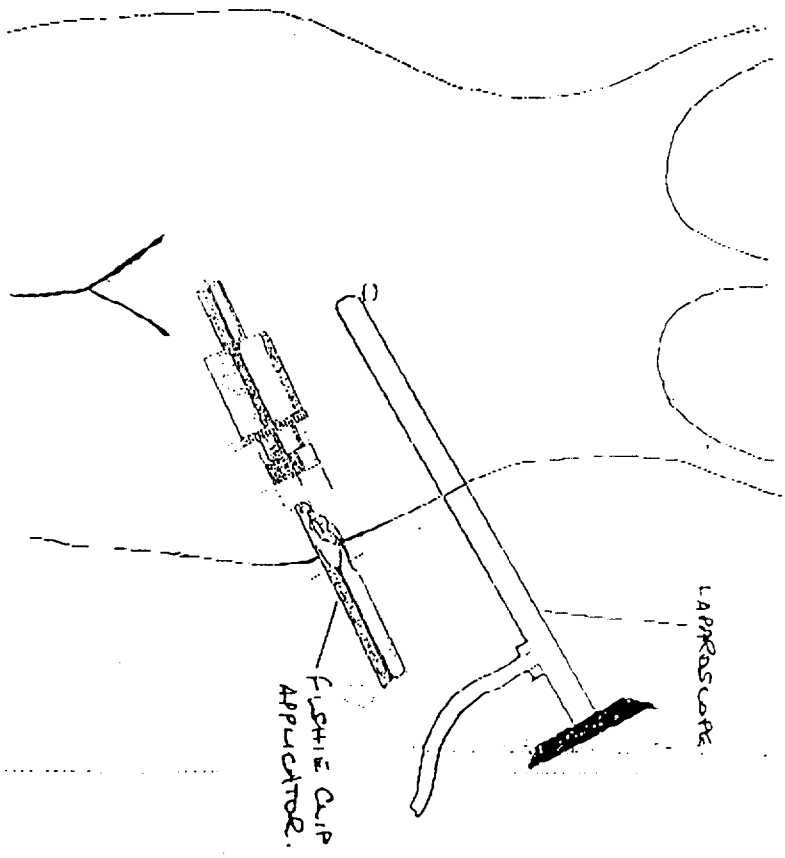
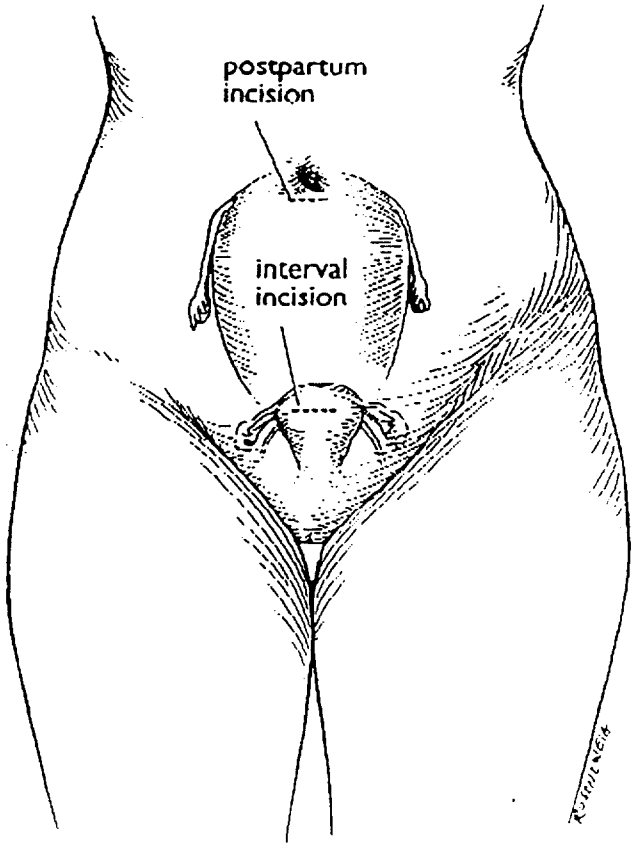


Fig 6.



Incision site: Postpartum and interval minilaparotomy

Diag 5.



Professional Labeling
Filshie Clip System™ for Tubal Occlusion

A contraceptive device for permanent female sterilization

CAUTION: Federal law restricts this device to sale, distribution, use by or on the order of a physician with appropriate training and experience.

TABLE OF CONTENTS

DESCRIPTION OF THE DEVICE

The Filshie Clip System includes the Filshie Clip and a series of applicators used to implant the clip.

Filshie Clip
The Filshie Clip consists of a rigid titanium body and a cross-linked silicone rubber lining. The upper and lower jaws are joined at one end by a hinge. The clip is provided sterile, packaged in a paper/polyester pouch. Attached to the open end of the upper jaw is a small 'no-touch' handle that is used to load the Clip into the applicator and then is detached from the Clip. The Clip is 13 mm long, 3.5mm wide and, when closed, 4mm high.

Applicators and accessories.
There are five applicators which may be used for application of the Filshie Clip.

- FC-4, intended for minilaparotomy, is 200mm in overall length with an effective shaft length of 100mm;
- FC-10A, intended for a single-incision laparoscopy (the operating laparoscope should have a working channel of 6 or 7 mm diameter, minimum), is 545 mm long overall with a shaft of 440mm in length and 5mm in diameter;
- FC-6A, also intended for single-incision laparoscopy and is designed for a operating laparoscope having a working channel of 8mm in diameter, minimum, is 520mm in length with a shaft 415mm long and 7.8mm in diameter;
- FC-7A, intended for dual incision laparoscopy and designed for use with the 7mm internal diameter Filshie trocar and cannula, is 355mm in length with a shaft that is 250mm long and 7mm in diameter; and
- FC-2A, intended for dual incision laparoscopy and designed for use with the 8mm internal diameter Filshie trocar and cannula, is 355mm in length with a shaft that is 250mm long and 8mm in diameter.

INDICATION AND USAGE

The Filshie Clip System is a contraceptive tubal occlusion device indicated for **permanent** female sterilization by occlusion of the fallopian tubes.

CONTRAINDICATIONS

The Filshie Clip should not be applied if any of the following conditions are present in the patient.

1. Pregnancy or suspicion of pregnancy.
2. Significant peritubular adhesions obscuring the portion of the fallopian tube to be occluded and impairing tubal mobility.
3. Acute pelvic inflammatory disease .
4. Salpingitis isthmica nodosa or chronic isthmic induration.

5. Hemoperitoneum or suspicion of ectopic pregnancy.
6. Any conditions contraindicating surgery or the use of anesthesia.

WARNINGS

(Adverse event rates reflect the results of the clinical study in which 5454 women were treated with the Filshie Clip. See Table 1).

1. Pregnancy
   a. Pregnancy, though infrequent, may occur after placement of the Filshie Clip (Table 2). Women with pre-existing pelvic inflammatory disease, obesity, and those in the early phases of a sterilization service program may be at increased risk of sterilization failure.
   b. Women sterilized postpartum or postabortion may be at increased risk of pregnancy. The pregnancy rate following tubal sterilization of postpartum patients is higher than that reported for interval patients. After two years the annual pregnancy rate for patients sterilized with the Filshie Clip was 1.7% for post-partum patients.
   c. Pregnancy following application of the Filshie Clip may be associated with applications in which the clip has not completely captured the fallopian tube or applications in which the clip has been placed on the wrong anatomical structure (such as the round or ovarian ligaments).

2. Ectopic Pregnancy
   a. Although rare, ectopic pregnancy has occurred following Filshie Clip sterilization (0.016% of subjects in clinical study). The possibility of ectopic implantation must be considered for any patient who becomes pregnant after application of the Filshie Clip.
   b. Special attention should be directed to patients with delayed menses, slight metrorrhagia, and/or unilateral pelvic pain to determine if ectopic pregnancy has occurred.

3. Unintended major surgery
   Trauma to pelvic organs, though infrequent, may occur during Filshie Clip application. This trauma may result in unilateral major surgical intervention (laparotomy) and repair. The need for unintended major surgery is apt to be more frequent in women with intra- abdominal adhesions, obesity, history of pelvic inflammatory disease, diabetes mellitus, and lung disease.

4. Trauma - Bleeding
   The normal closure of the Filshie Clip may cause immediate transection with bleeding in a small number of cases. A second clip may be applied on the proximal (uterine) side of the lesion, but with a much slower closing action to ameliorate the bleeding. Transection of the tube may lead to unintended major surgery.

5. Technical failures
   a. Technical failures which require changing from the planned procedure to another sterilization procedure or abandonment of the sterilization procedure, although rare, may occur during a Filshie Clip procedure. Technical failures are more likely among women

47

with enlarged uteri (post-partum) or other pre-existing patient factors such as peritubular adhesive disease or obesity.

b. Technical failures have been associated with equipment malfunction. Both the operator and support personnel should be familiar with the operation, sterilization, and maintenance of the Filshie Clip applicator and associated devices prior to use.

6. Infection
   a. Pelvic infection may occur as a result of sterilization with the Filshie Clip (0.1%). This can lead to tuboovarian abscesses, endometritis, or salpingitis. Aerobic and anaerobic studies, including cultures for Chlamydia trachomatis should be conducted when pelvic infection is suspected.
   b. Incisional infection may occur following tubal sterilization (1.3%).
   c. Urinary tract infections may occur following tubal sterilization (1.0%).

7. Clip Expulsion, Foreign Body Reactions, and Asymptomatic Migration
   Instances of clip expulsion per urethra, vaginal cuff and bowel, as well as foreign body reactions have been reported (3 expulsions and 2 foreign body reactions were reported in 5,326 women). Three instances of apparently asymptomatic migration of the clip were observed as incidental findings, but the frequency of this event is not known.

PRECAUTIONS

1. Patient evaluation
   A complete medical history should be obtained to determine conditions that might influence the selection of the procedure, or are absolute or relative contraindications to surgery. A routine physical examination should be performed noting the integrity of the pelvic organs and, if indicated, a pregnancy test to determine whether there is an existing pregnancy. The patient should be evaluated for pelvic inflammatory disease, cardiovascular disease, severe ileus, acute peritonitis, previous pelvic surgery, significant hemoperitoneum and other conditions which contraindicate surgery of the use of anesthesia.

2. Patient Counseling
   a. Prior to any sterilization procedure being performed, the patient should be fully informed about alternative methods of contraception, the possible side effects of the procedure, any complications which may arise during and following the procedure and the risks and benefits associated with sterilization in general and the Filshie Clip procedure in particular. The patient should fully understand that this is a **permanent** procedure. In addition, the patient should be encouraged to discuss openly and fully any questions she may have concerning the Filshie Clip.
   b. The patient should be advised that if any post-operative symptoms are severe or persist, she should see her physician.
   c. The patient should be informed that sterilization will not prevent sexually transmitted diseases (STDs). Additional precautions against STDs must still be taken after sterilization.

3. Clinical Usage
   a. For each procedure, use only clips enclosed in the sealed, sterile package.
   b. Check the operation of the Applicator prior to use (see operating instructions).
   c. Physicians should be thoroughly familiar with the Filshie Clip System, tubal sterilization procedures, and management of tubal sterilization complications before attempting its use. The supporting staff should be familiar with the maintenance, proper assembly and disassembly, cleaning, and sterilization of the Filshie Clip applicator.
   d. Improper loading and testing of the applicator may result in Filshie Clips being either inadvertently discharged into the peritoneal cavity or incorrectly placed. Refer to the Operator's Instructions for the proper method for inserting the clips into the applicator, and the recommended course of action for an incorrectly placed clip.
   e. Physicians are cautioned that they should confirm the location of the pelvic organs before Filshie Clip application to prevent inadvertent application to an inappropriate anatomical structure such as the round or ovarian ligament.
   f. The safety and effectiveness of the Filshie Clip for permanent sterilization has only been tested and clinically evaluated using the Femcare Ltd. Filshie Clip Applicators. Applicators from other manufacturers should not be used.

4. Long Term Implantation and Sequelae
   a. The silicone elastomer and titanium used in the manufacture of the Filshie Clip are generally regarded as safe materials for human implantation. Although no adverse toxic or tumorigenic effects due to the device or its materials have been reported, the effects of long term implantation are unknown. The clips has been show to be compatible with MRI procedures.
   b. The long term effects of tubal sterilization on women are unclear. Several uncontrolled studies suggest that women undergoing tubal sterilization may be prone to gynecological problems. More recent controlled studies report that sterilization does not cause any long term effects. The rates of hospital referral for gynecological or psychiatric condition appear to be similar for women undergoing tubal sterilization and women whose husbands underwent vasectomy.
   c. In the event of a subsequent hysterectomy, it has been recommended that the clips be removed, as leaving them in may predispose the patient to a later expulsion[1].
   d. Testing to ensure compatibility with Magnetic Resonance Imaging (MRI) has been conducted using a 1.5 Tesla magnet. No clinically significant attractive forces were observed at that field strength. However, the presence of the clips produces an MR artifact which will obscure imaging of local tissue.

ADVERSE EFFECTS

The following adverse effects have been reported with the use of the Filshie Clip (see Table 1).

pregnancy (0.46%); ectopic pregnancy (0.016%); clip migration or expulsion (0.13%); misapplication to ovarian ligament, broad ligament, omentum, bowel, tubal serosa, cornual or broad ligament (0.05%); pain and cramping (35.7%);

Other adverse effects reported from surgical procedures to implant the Filshie Clip include the following:

> musculoskeletal pain (6.0%); adnexal pain/enlargement/infection (5.0%); incisional inflammation, bleeding, abscess or pain (4.4%); nausea/vomiting (4.0%); keloids (3.9%); headache (3.0%); serous discharge (2.8%); vaginitis (1.1%); urinary tract infection (1.0%); and hematoma (1.0%).

Menstrual pattern changes, involving the amount of blood flow, duration of flow, cycle regularity and cycle length, and dysmenorrhea, may occur following tubal sterilization. Menstrual disturbances not present at baseline in women who received the Filshie Clip were reported as follows: 6.9% excessive flow; 0.7% menorrhagia; 1.4% vaginal bleeding; 2.6% severe dysmenorrhea; and 0.6% severe intermenstrual pelvic pain. These effects have been reported to be associated with other methods of tubal sterilization, and they often disappear within a year following sterilization.

Table 1. Adverse Experiences Ever Occurring in > 0.5% of All Patients Post-Surgery

Adverse Events by Body System	Filshie Clip (N = 5454) No	%	Other Tubal Occlusion Device/Method (N = 3845) No.	%
Digestive				
Nausea/vomiting	235	(4.3)	155	(4.0)
Musculoskeletal				
Back pain	32	(0.6)	23	(0.6)
Shoulder pain	295	(5.4)	212	(5.5)
Nervous/psychiatric				
Headache	164	(3.0)	89	(2.3)
Skin				
Keloid	214	(3.9)	196	(5.1)
Serous discharge	152	(2.8)	121	(3.1)
Primary incision inflammation	138	(2.5)	96	(2.5)
Wound abscess	29	(0.5)	36	(0.9)
Wound bleeding	23	(0.4)	21	(0.5)
Hematoma	55	(1.0)	35	(0.9)
Incomplete dehiscence	24	(0.4)	30	(0.8)
Incision pain	81	(1.5)	93	(2.4)
Urogenital				
Vaginitis	62	(1.1)	53	(1.4)
Vaginal abnormality	29	(0.5)	25	(0.7)
Dysplasia	32	(0.6)	17	(0.4)
Uterine abnormality	51	(0.9)	29	(0.8)
Menses (for condition not present at baseline)				
Excessive flow	379	(6.9)	209	(5.4)
Severe dysmenorrhea	144	(2.6)	57	(1.5)
Severe intermenstrual pelvic pain	35	(0.6)	16	(0.4)
Menorrhagia	37	(0.7)	7	(0.2)
Vaginal bleeding	79	(1.4)	65	(1.7)
Infection in adnexa	24	(0.4)	24	(0.6)
Tender/enlarged adnexa	143	(2.6)	139	(3.6)
Pelvic pain	1949	(35.7)	1652	(43.0)
Adnexal pain	109	(2.0)	91	(2.4)
Urinary tract infection	57	(1.0)	29	(0.8)

Note: Multiple complaints may be reported per woman

CLINICAL STUDIES

For the 5754 women who were enrolled in the eleven prospective clinical trials reported in the premarket approval application (PMA) and who were sterilized using the Filshie Clip system, only 22 pregnancies were reported. Only one ectopic pregnancy was reported. A list of the adverse events that were reported in the clinical study is provided in Table 1.

Four of the clinical studies were designated "pivotal studies". These studies are prospective, randomized, controlled clinical studies comparing the Filshie Clip to the Hulka Clip or the Falope Ring. The method of application was either laparoscopy or minilaparotomy. The 12-month followup results are shown in Table 2. There was no statistically significant difference between the failure rates for the Filshie Clip as compared to the Hulka Clip or the Falope Ring.

Table 2. Filshie Clip System - Gross Cumulative Life-Table Pregnancy Rates

Pooled Pivotal Studies	Months of Follow-up	Pregnancy Rate (Standard Error) per 100 Women per Year	
		Filshie Clip System™	**Comparison Device**
Filshie vs. Hulka Clip[1]	12	**0.1 (0.1)** n=1063 % completing = 68.7%	**0.7 (0.3)** n=1062 % completing = 67%
Filshie vs. Falope Ring[2]	12	**0.2 (0.1)** n=1378 % completing = 81.9%	**0.2 (0.1)** n=1355 % completing = 82.4%

[1]The Hulka Clip is also known as the Wolf Clip.
[2]The Falope Ring Band is also known as the Tubal Ring and the Yoon Ring.

Results from a single study suggest that the Filshie Clip may be less effective than the Pomeroy method in post-partum women. Of 1400 women who were enrolled in a 24-month study, nine reported pregnancies in the Filshie group, and two in the Pomeroy group.

Table 3. Pregnancy Rates for Birth Control Methods

Each value given is an estimate of the percent of women likely to become pregnant while using a particular contraceptive method for one year. These estimates are based on a variety of studies.

"**Lowest Expected**" rates indicate that the method was used correctly with every act of sexual intercourse but failed anyway (e.g., remembered to take daily hormonal contraceptive pill, but became pregnant).

"**Typical**" rates indicate that the method either was used incorrectly, was not used with every act of sexual intercourse, or failed during use (e.g., forgot to take daily hormonal contraceptive pill, and became pregnant).

Method	Lowest Expected	Typical
Sterilization:		
Male Sterilization	0.1%	0.15%
Female Sterilization	0.4%	0.4%
Hormonal Methods:		
Implant *(Norplant™)*	0.09%	0.09%
Hormone Shot *(Depo-Provera™)*	0.3%	0.3%
Combined Pill *(Estrogen/Progestin)*	0.1%	3%
Minipill *(Progestin only)*	0.5%	3%
IUDs:		
Copper T	0.6%	0.8%
Progesterone T	1.5%	2%
Barrier Methods:		
Male Latex Condom	3%	12%
Diaphragm	6%	18%
Cervical Cap *(no previous births)*	9%	18%
Cervical Cap *(previous births)*	26%	36%
Vaginal Sponge *(no previous births)*	9%	18%
Vaginal Sponge *(previous births)*	20%	36%
Female Condom	5%	21%
Spermicide *(gel, foam, film)*	6%	21%
Natural Methods:		
Withdrawal	4%	19%
Natural Family Planning *(calendar, temperature, symptothermal)*	1-9%	20%
No Method:	85%	85%

Data adapted from: R.A. Hatcher, J. Trussell, F. Stewart, et al. (eds.), Contraceptive Technology, 16th Revised edition, New York, NY: Irvington Publishers Inc., Chapter 5 (1994).

HOW SUPPLIED:

Twenty (20) pairs of Filshie Clips and prescribing information are contained in a single carton. Each pair is contained in a procedure package consisting of one pair of Filshie Clips in a sterile peelable pouch.

A procedure kit consisting of the applicator, trocar and cannula, cleaning brush and instruction manual can be purchased separately.

INSTRUCTIONS FOR USE:

[diagram]
The Filshie Clip

Shown below is the appearance of the Filshie Clip at different stages of operation

[diag 1] [diag 2] [diag 3] [diag 4] [diag 5]

Diag 1: Fully open in the pack with the loading handle fitted.
Diag 2: Partially open, as it sits in the loaded applicator.
Diag 3: Half closed, as it goes down cannula.
Diag 4: Partially secured, giving a temporary grip on tube; reopenable at this stage
Diag 5: Permanently secured after force applied to applicator. Latching has occurred and the Clip cannot be opened or removed.

1
ASSEMBLING THE EQUIPMENT

[diagram]
The Filshie Clip Applicator

NOTE
Each applicator is individually calibrated by the manufacturer. **No adjustments should be made to an applicator by unauthorized persons.** Calibration and recalibration are critical operations which must only be performed by the manufacturer or their appointed agent. Always check that the serial numbers on the handle assembly and the shaft of the applicator are the same. If they are not, **DO NOT USE**

Only the Filshie Clip Applicators manufactured by Femcare should be used to implant the Filshie Clip.

THE APPLICATOR.

APPLICATOR ASSEMBLY

Using a clockwise motion, screw the handle assembly to the shaft of the applicator. Use firm but gentle pressure to ensure a finger tight connection.
NEVER USE EXCESSIVE FORCE AS THIS MAY CAUSE CROSS-THREADING, PERMANENTLY DAMAGING THE APPLICATOR.

[diagram]

CHECK ALIGNMENT

[diagram]

When the applicator is assembled the moveable jaw should be approximately in line with the finger bar. 30° to the left or right is acceptable.

TEST APPLICATOR

[diagram]

Check that the applicator operates smoothly by squeezing the finger bar a few times.

If either alignment or operation is not satisfactory return the applicator to the manufacturer or appointed agent.

2.
LOADING THE FILSHIE CLIP USING THE "NO TOUCH" TECHNIQUE

Pick up the Clip using the plastic no touch handle already attached to the Clip. Using this "No Touch" technique, slide the bottom of the Clip along the floor of the applicator jaw until the Clip is within the retaining lip.

[diagram]

Detach the "No Touch" handle from the Clip, as shown in the diagram, then discard it.
TO MAINTAIN STERILITY, NEVER TOUCH THE CLIP.

[diagram]

3.
CHECK LOADING 1,2,3.

1. Check that the bottom portion of the Clip lies perfectly flat on the floor of the applicator jaw, not rising up at the back or front. [diagram]

2. Check that the upper portion of the Clip is located between the side guides of the applicator's moveable jaw. [diagram]

3. Check that the front end of the Clip lies directly behind the front stop on the applicator. [diagram]

Either of the two incorrect loadings above will produce distorted Clips which may lead to pregnancy.

4.
ADJUST FRICTION WASHER ON CANNULA

[diagram]
Trocar and Cannula

Adjust the position of the friction washer, by sliding it along the shaft of the cannula, to suit the anticipated required depth of entry into the abdomen for each patient. [diagram]

Insert the trocar into the cannula, taking care not to damage the end seal. [diagram]

5.
INSERTING THE APPLICATOR THROUGH THE CANNULA
(The applicator is suitable for both right and left handed operation)

In order to pass the loaded applicator through the cannula it must be half closed. This is achieved by gently squeezing the finger bar until **the moveable jaw is in the half-closed position (diagram A).** The finger bar should be squeezed just enough to allow smooth passage of the applicator through the cannula. If you squeeze the finger bar too tightly you may cause the Clip to lock prematurely or to become distorted so that it may fail to lock properly. This maneuver should be practiced several times before clinical use. When the rubber seal reaches the index mark etched on the shaft, the mouth of the applicator will have emerged at the far end of the cannula.

Maintain gentle pressure to keep the Clip half closed until you can see it through the laparoscope. Slowly release the finger bar and the Clip will re-open ready for application.

[A series of 4 diagrams accompanies the text above]

6.
MANIPULATING THE FALLOPIAN TUBE

It is possible to manipulate the Fallopian tube for identification purposes by gently using the loaded applicator as a pair of soft forceps, being careful not to take the finger bar past the half-closed position. Heavy handed manipulation must be avoided as this could result in the Clip being dislodged from the applicator. The use of uterine elevators may be helpful in exposing the tube, particularly so in the case of retroverted uteri.

7.
APPLYING THE FILSHIE CLIP

** The Clip is not designed to be removed once it is placed - the physician should be certain of the exact placement prior to closing the Clip. **

1. Inspect the tube thoroughly.
2. Ensure that the Clip can accommodate the whole diameter of the tube.
3. Place the Clip on the isthmic portion of the tube, 1-2cm from the cornu.
4. If there is any doubt about the security of the Clip, a second Clip may be placed immediately adjacent to the first Clip, on the uterine side.
5. In the unlikely event of the tube being too large for the Clip, use an alternative method of tubal occlusion.

[diagram]

Having established the best location for the Clip, the applicator should be re-opened and advanced a few millimeters to move the tube gently to the back of the Clip, close to the hinge.

[2 diagrams showing correct and incorrect]

Lock the Clip into position by applying firm, but gentle pressure on the finger bar in a smooth action until the stop is reached. Do not use an abrupt action or the tube may be transected. Should this happen, a second Clip may be applied on the proximal (uterine) side of the transection. This should be done very slowly. It is quite noticeable, but quite normal, for the muscle of the tube to "give" during Clip application. When the Clip is locked in position, release the finger bar and the Clip will free itself automatically from the applicator. [diagram]

8.
FINAL INSPECTION OF THE APPLIED CLIP

Using the empty mouth of the applicator as a probe, inspect the secured Clip to confirm that the entire tube has been captured, the upper jaw has been compressed and is securely locked under the nose of the lower jaw (diagram C) and the Clip is in a good position on the correct anatomical structure (not on either the round or ovarian ligament).

9.
REMOVAL OF THE APPLICATOR AND DESUFFLATION

Before the applicator is removed from the abdomen through the cannula it must be returned to the half-closed position. [diagram]

When both tubes have been clipped, inspected and the applicator finally withdrawn from the abdomen, desufflation of the pneumoperitoneum is necessary. This can be achieved by either introducing the desufflation key into the cannula to open the trapdoor valve or by unscrewing the

cannula barrel cap assembly to allow the dissipation of the gas. The cannula may then be removed. [diagram]

The applicator, trocar and cannula may then be cleaned and resterilized.

10.
DISASSEMBLY OF THE EQUIPMENT FOR CLEANING

[A series of 5 diagrams accompanies the following text]

Applicator (both 7mm and 8mm).
Unscrew the handle assembly from the shaft using an counter-clockwise motion. Remove the silicone seal tube from the exposed end of the push rod. If the seal is undamaged it may be reused later.

Cannula for 8mm applicators.
Remove the end cap seal and if it is undamaged, retain it for reuse later. Unscrew the barrel cap assembly from the body of the cannula, being careful not to damage the seals.

Cannula for 7mm applicators.
Unscrew the knurled ring at the end of the cannula and remove the silicone seal gasket. If it is undamaged retain it for reuse later. Unscrew and remove the large knurled ring and then separate the trapdoor assembly from the body of the cannula by pulling and twisting.

If any of the seals are damaged or have deteriorated, refer to section 15.

11.
CLEANING THE SUB-ASSEMBLIES

The ideal method of cleaning the various parts is by total immersion in an ultrasonic bath using a suitable detergent (check with your sterile supply department), followed by thorough rinsing and flushing with clean water. If this method is used, the cannula trapdoor should be propped open with a small rubber bung to allow full penetration of the cleaning fluid and rinsing water. If these cleaning facilities are not available, the sub-assemblies may be cleaned manually in a suitable detergent solution using the brush provided. Particular attention must be paid to the areas that may act as a trap for blood and tissue fluids. The cannula trapdoor should be held open while brushing the underside and the areas to which it seals. After cleaning with the detergent solution, the sub-assemblies should be thoroughly rinsed and flushed with clean water. It is inevitable that blood and tissue fluids will become trapped inside the applicator main tube during use. The cleaning adapter supplied will help you to flush these contaminants away, simplifying the cleaning process. The adapter, when screwed onto the applicator main tube section, allows you to force cleaning fluid or water down the shaft to remove debris that has been loosened by the initial cleaning processes, using a standard Luer Lok syringe. Regardless of which cleaning method is used, as much excess water as possible must be shaken off the sub-assemblies before they are reassembled for sterilization.

12.
PREPARATION PRIOR TO STERILIZATION

Applicator.
Replace the seal tube over the exposed push rod on the applicator shaft, ensuring that it goes over the shoulder of the main tube and close up to the threaded portion. [diagram]
When correctly fitted the seal tube should not be stretched.
Do not screw the handle assembly onto the shaft of the applicator.

Cannula (7mm).
Reassemble the trapdoor assembly and the main body of the cannula for 7mm applicators ensuring that the large knurled ring is screwed firmly into place. Replace the end seal gasket and screw the small knurled ring firmly into place to retain it. **Do not insert the trocar into the cannula.**

Cannula (8mm).
Replace the end cap seal on the cannula for 8mm applicators and screw the barrel cap assembly onto the body of the cannula. The barrel cap assembly should be screwed firmly into place to ensure a gas tight seal between the two parts. **Do no insert the trocar into the cannula.**

13.
STERILIZATION

The applicators should be sterilized by autoclaving at 121°C for 15 minutes

The applicator should be sterilized in two parts. The cannula should be assembled but the trocar kept separate. These sub-assemblies should be suitably packed for the sterilization method to be used and should be protected from any rubbing or knocking against other items during the process.

Do not use a dry heat sterilization process or wet chemical sterilizing agents containing glutaraldehyde. Either of these will cause deterioration of the applicator.

14.
THE MINILAP APPLICATOR

This instrument is used when the tubal occlusion is to be carried out using the minilaparotomy approach. This approach is particularly recommended for use in the immediate postpartum or postabortum period.

The applicator is presented as a single piece assembly which cannot be disassembled. The loading of the Clip and the principles of operation are identical to the dual incision range. Since

no pneumoperitoneum is induced in the minilaparotomy technique, the applicator is not fitted with a gas seal tube.

Cleaning.
The cleaning and sterilization of the Minilap applicator is similar to that of the dual incision range except that no disassembly or reassembly is required. The applicator is not fitted with a gas seal tube, but in all other respects, customer's maintenance is similar to the dual incision range.

15.
PERIODIC REPLACEMENT OF SEALS

When any of the old seals show signs of damage or wear, they must be replaced.

Applicators.
Use only genuine Filshie Clip Applicator replacement parts as others have not been tested and shown to work properly. For disassembly and replacement of the applicator seal tube (FE 011) see previous sections 10 and 12.

8mm Cannula.

[diagram]

There are three seals on the 8mm cannula which must be inspected for signs of deterioration or damage and replaced if necessary.

Cap seal (code FE 006):- Simply pull off the old seal and push on a new one.
Black "O" ring (code FE 008):- This is to be found in the barrel cap assembly. Unscrew the knurled ring and pull off the cap assembly. The black "O" ring can be found in the outer groove on the underside of the assembly. The old "O" ring may need to be dug out with the aid of a sharp instrument. **Exercise caution.** Clear any debris from the groove using the cleaning brush supplied in the kit. Gently press the new "O" ring into the groove. When properly fitted there should be no gas escape.
Trapdoor seal (code FE 007):- This is to be found in the body of the barrel cap assembly under the trapdoor flap. Dig out the old seal using a sharp instrument. **Exercise caution.** Clear any debris from the groove using the cleaning brush supplied in the kit. Replace with a new seal.

Caution:
The trapdoor seal has one domed surface and one flat surface. The flat surface must be at the bottom of the groove. If inserted upside down the seal may be dislodged from its groove during use.

[2 diagrams showing correct and incorrect fitment]

Gently press the new trapdoor seal into the groove. Reassemble by screwing the barrel cap assembly back onto the cannula shaft until finger tight.

7mm Cannula.

[diagram]

There are two seals on the 7mm cannula which must be inspected for signs of deterioration or damage and replaced if necessary.

Silicone seal gasket (code FE 021):- Unscrew the small knurled ring. Remove the old seal from its seating. Replace with a new seal. Ensure that the new seal is seated properly. Replace the knurled ring.
Silicone trapdoor seal (code FE 070):- Unscrew the large knurled ring. Hold the trapdoor flap open. Remove the screw on the top side of the dome using a **clockwise** motion. This liberates the dome. Remove the seal. Clear any debris with the cleaning brush provided in the kit. Replace with a new seal ensuring that it is seated correctly. Replace the dome and hold it in position with one finger and tighten the screw using a **counterclockwise** motion. **Caution: Do not over tighten the screw as this may distort the seal leading to gas loss.** When satisfied that the seal is correctly in place, replace the trapdoor assembly into the cannula shaft and refit the large knurled ring.

SEAL CHECK ON CANNULAS.
To test if the seals are correctly in position after replacement, carry out the following procedure: Dip the top end of the cannula in a beaker of water. Connect a piece of soft tubing to the shaft of the cannula and blow down the tubing. If air bubbles are detected in the water at a rate greater than one bubble per second then the seals need replacing or reseating.

16.
OTHER MAINTENANCE

If the point of the trocar becomes slightly blunted or chipped it may be restored using the oilstone provided. **This must be done with care.** The trocar for use with 8mm applicators has a replaceable screw-in tip which may be replaced by the customer. 7mm trocars or 8mm tips that have suffered major damage should be returned to the manufacturer or their appointed agent to be reground.

NO OTHER MAINTENANCE OR ADJUSTMENT should be performed other than by the manufacturer or their appointed agent. The applicator is a finely calibrated instrument and no liability will be accepted by the manufacturer for problems or failures arising as a result of any unauthorized repair or adjustment. Like all mechanical equipment, the Filshie equipment will deteriorate with use and age.

It is strongly recommended that the equipment is serviced and recalibrated by the manufacturer or their appointed agent at least once a year depending on your usage rate.

17.
REPLACEMENT PARTS

The following parts are available. Please contact your local sales representative or dealer.

Spare parts for 7mm applicators, trocars and cannulas.

FE 027:- Cannula Friction Washer
FE 021:- 7mm cannula Silicone Seal Gasket - white or grey
FE 070:- 7mm cannula Silicone Trapdoor Seal (captive)-white or grey
FE 011:- Applicator Silicone Seal Tube
FE 012:- Oil Stone
FE 013:- Cleaning Brush

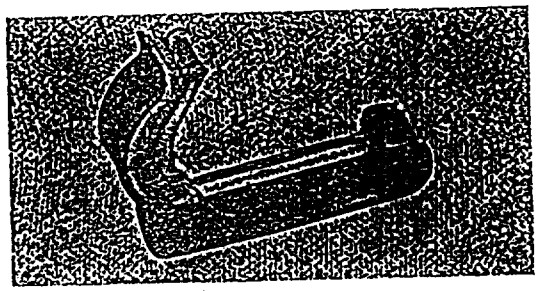
Spare parts for 8mm applicators, trocars and cannulas.

FE 004:- Replaceable trocar tip
FE 005:- 8mm cannula Friction Washer
FE 006:- 8mm cannula Barrel Cap Seal
FE 007:- 8mm cannula Silicone Trapdoor Seal
FE 008:- 8mm cannula Black "O" Ring
FE 011:- Applicator Silicone Seal Tube
FE 012:- Oilstone
FE 013:- Cleaning Brush

REFERENCES

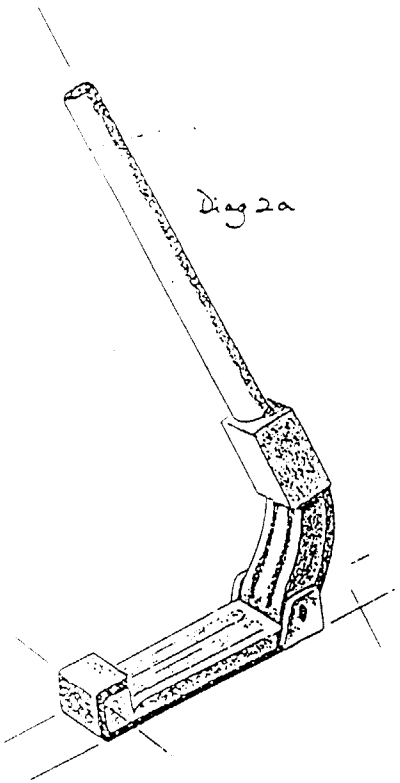
1 Barker, G.H. and D.W. Roberts. Spontaneous extrusion of Hulka-Clemens spring-loaded clips after vaginal hysterectomy: Two case reports. British Journal of Obstetrics and Gynaecology. 84:954-5, 1977.

Diag 1



The Filshie Clip®

Diag 2a



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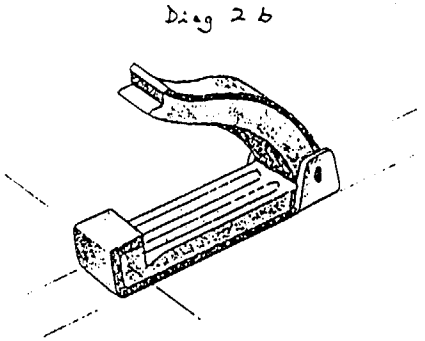

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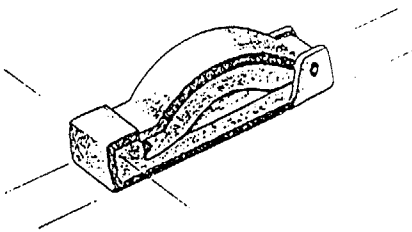

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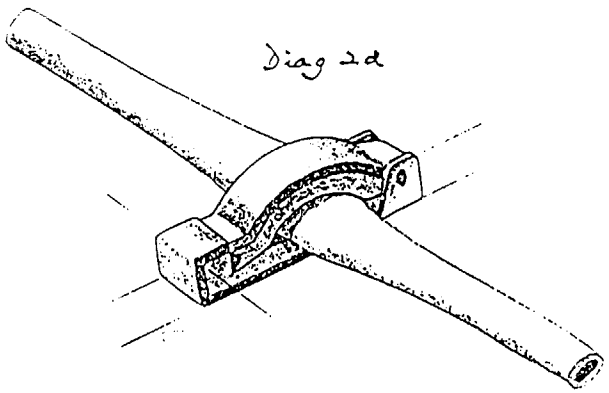
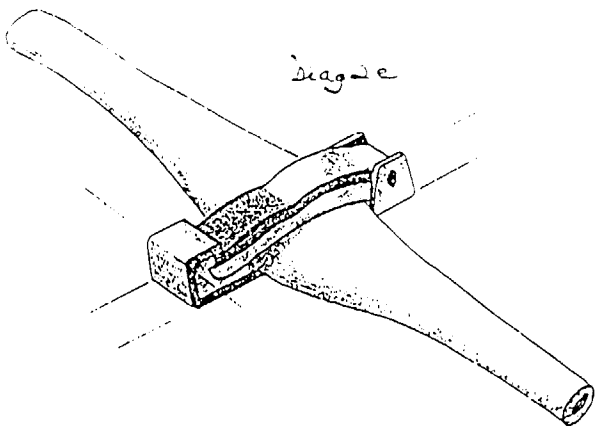


Diag 2e



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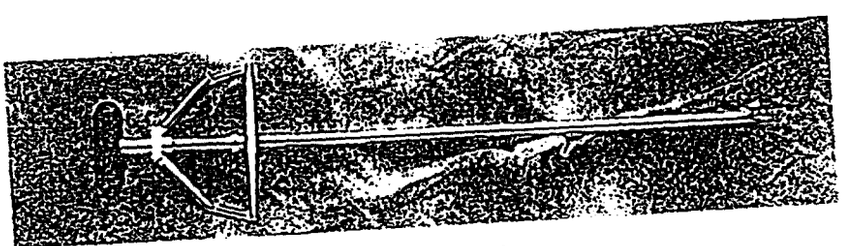
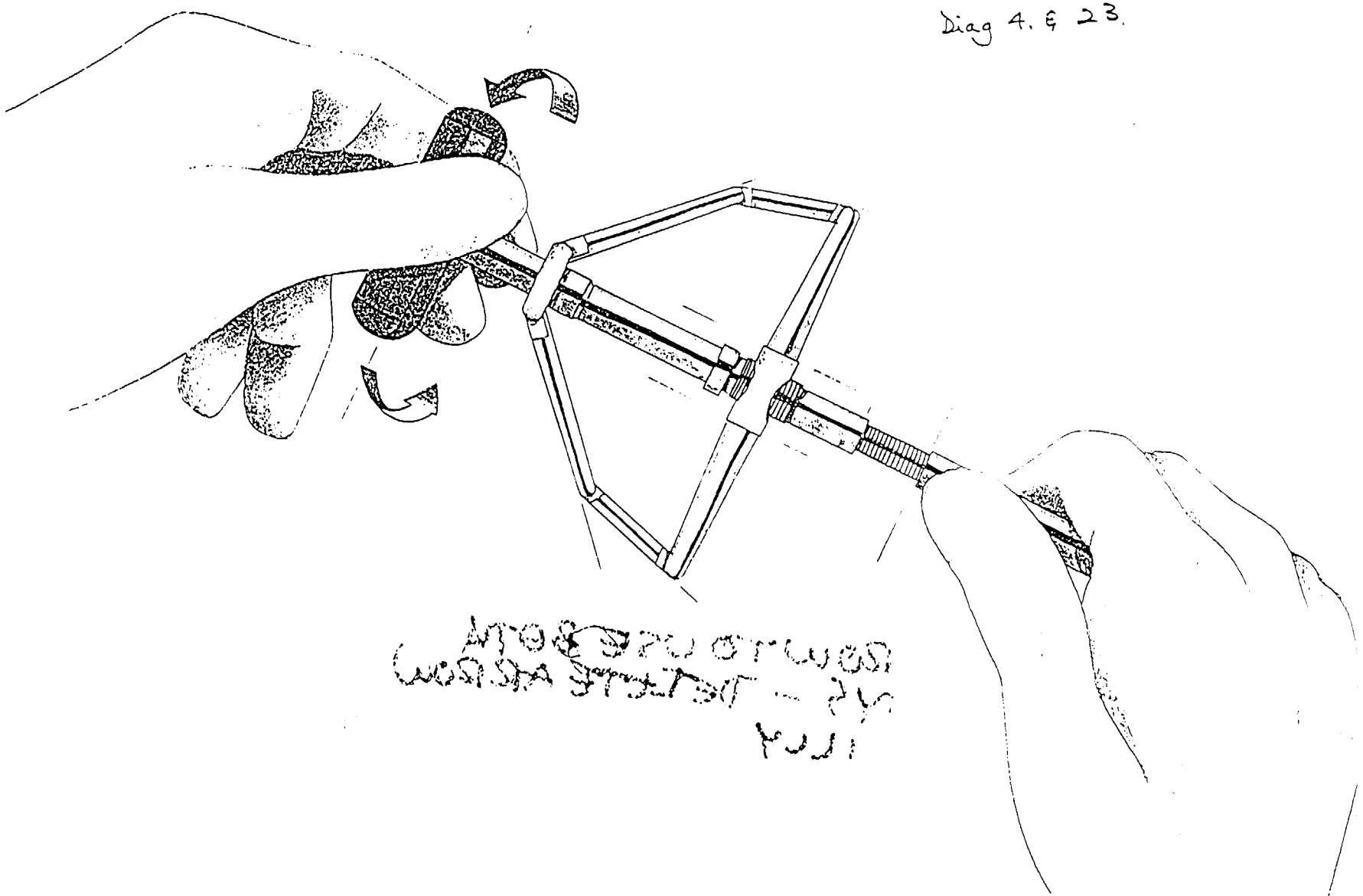


The Filshie Clip® Applicator

Diag 4. § 23.



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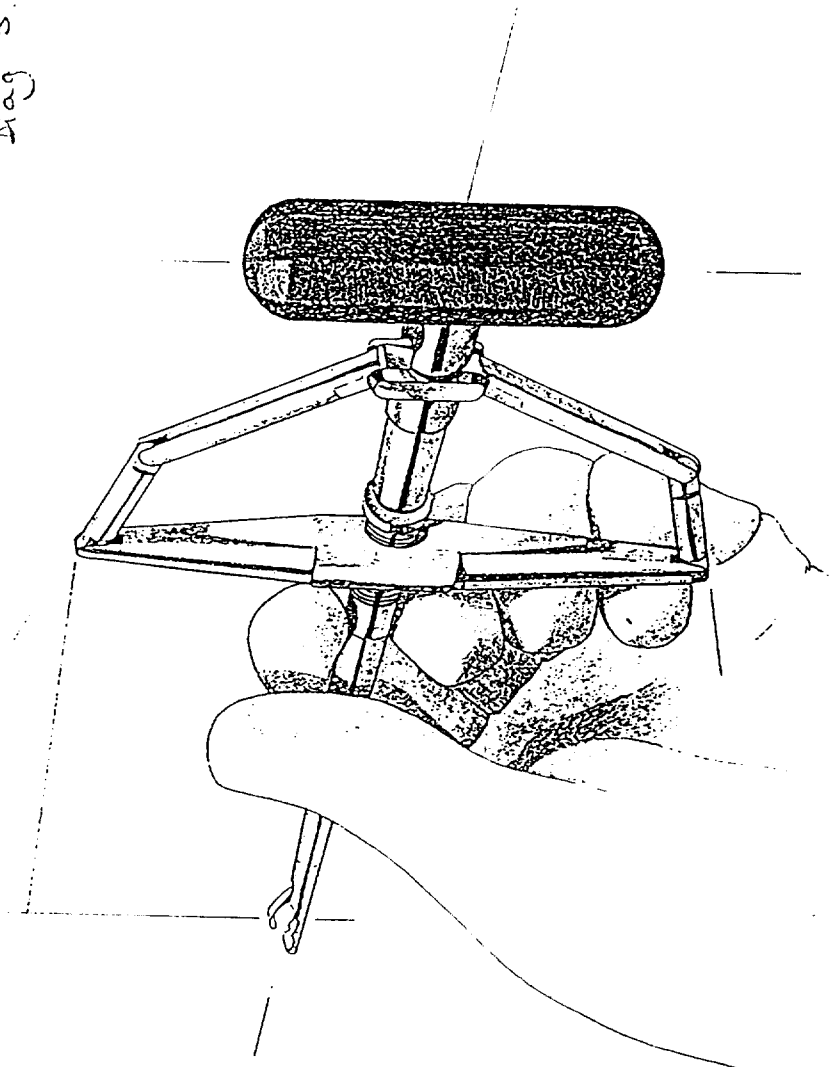


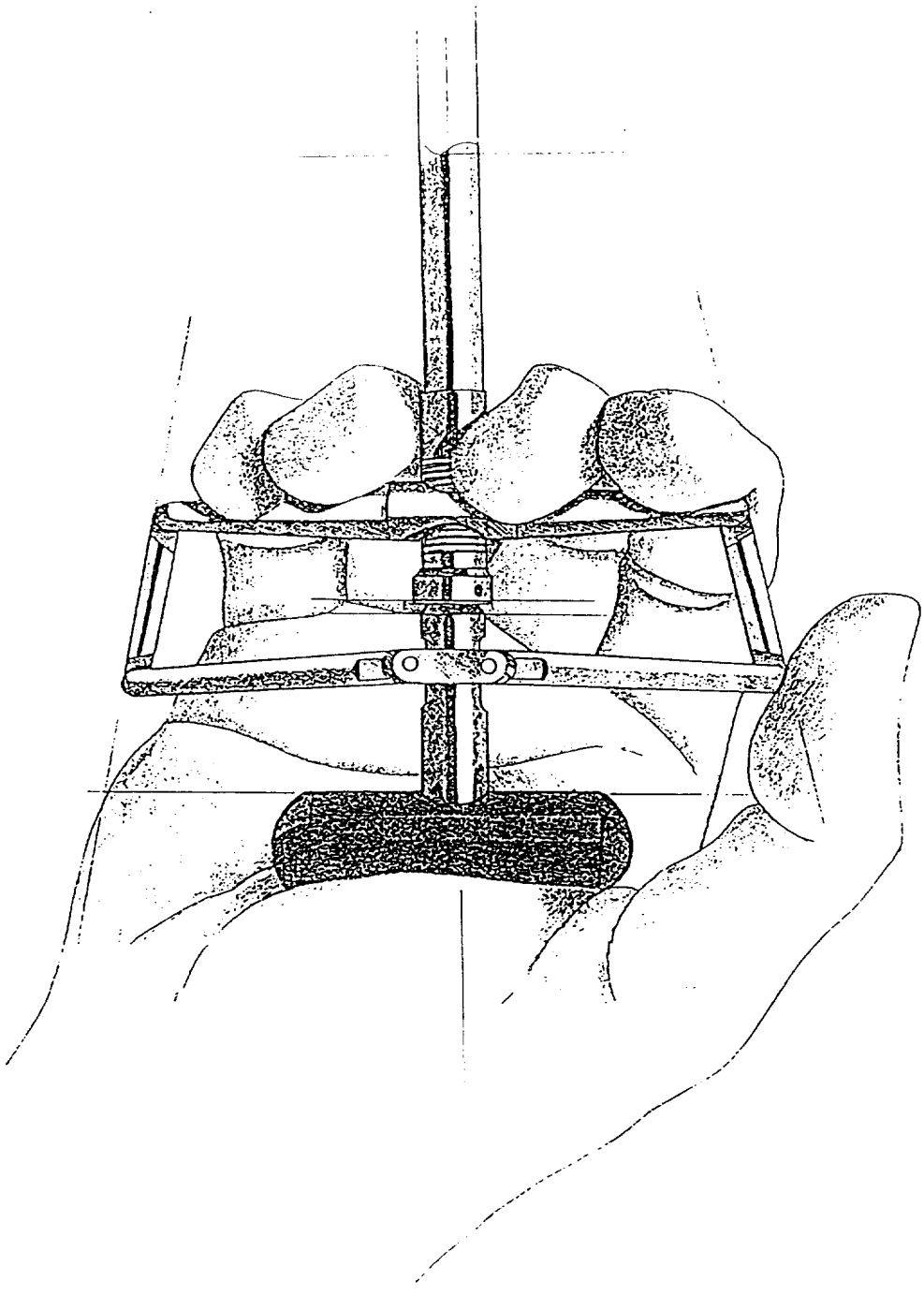
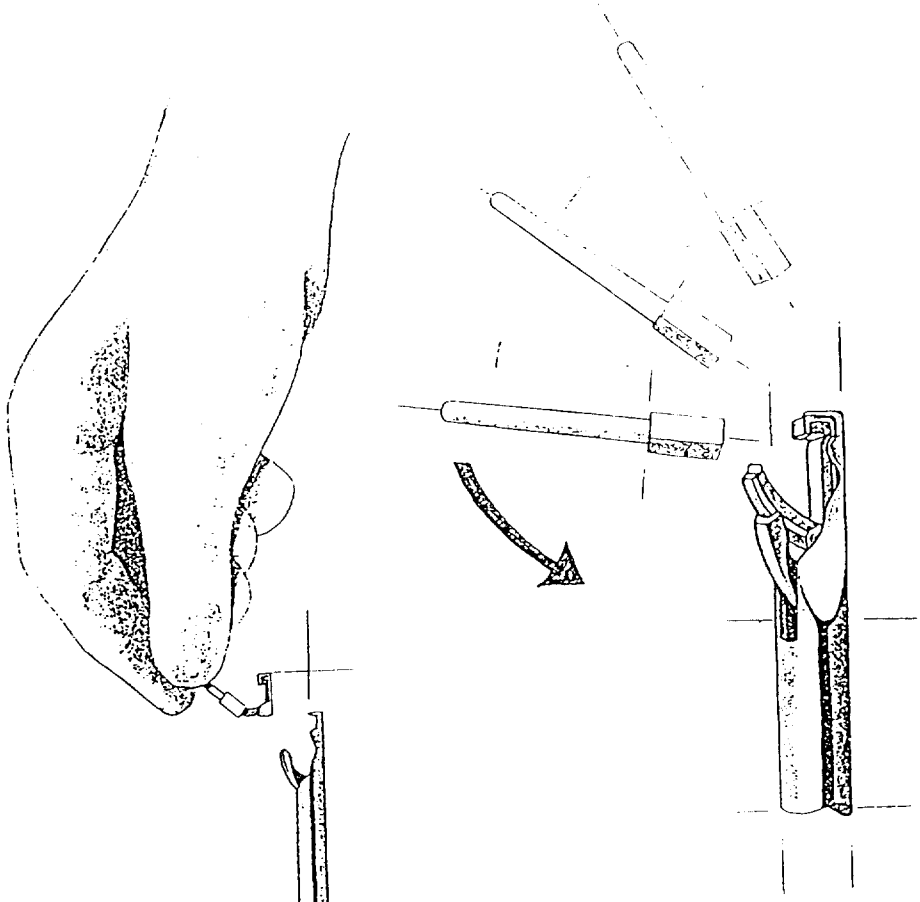
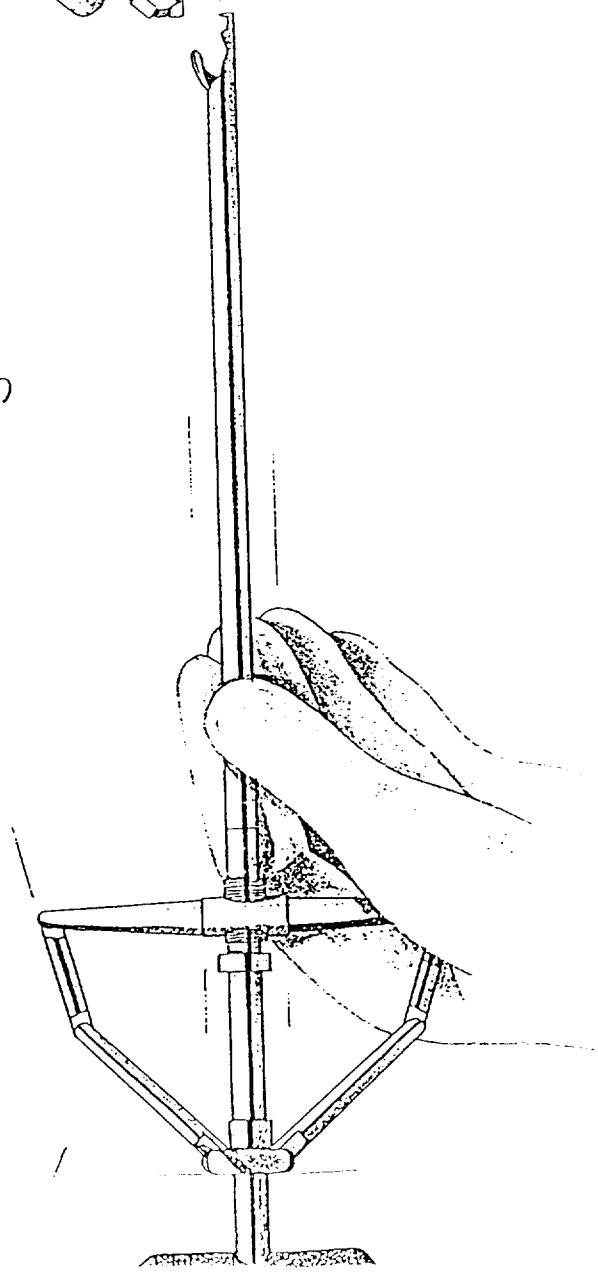


Fig 6



diag 8.



diag 7

Diag 9
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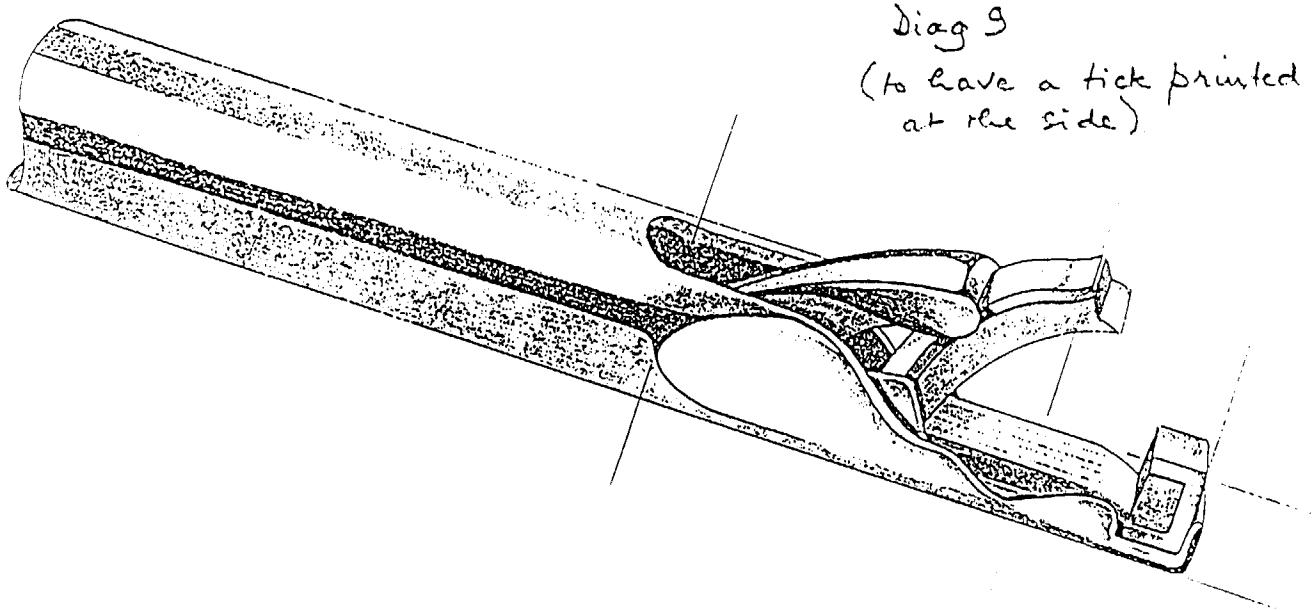

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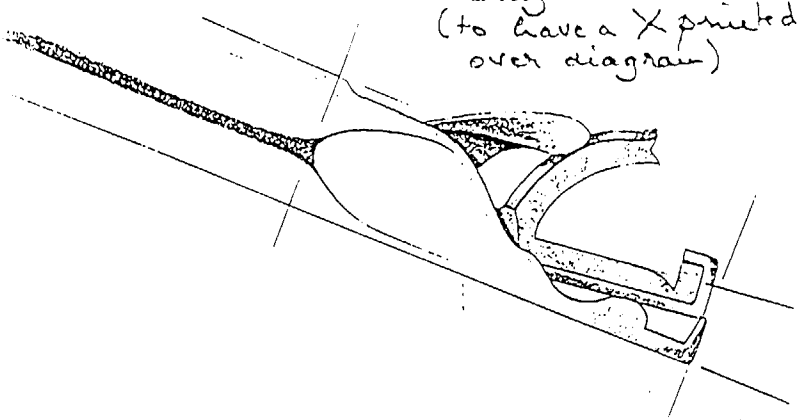

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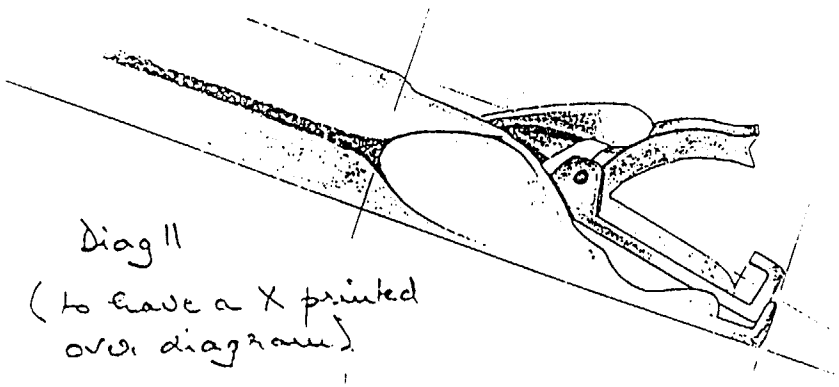

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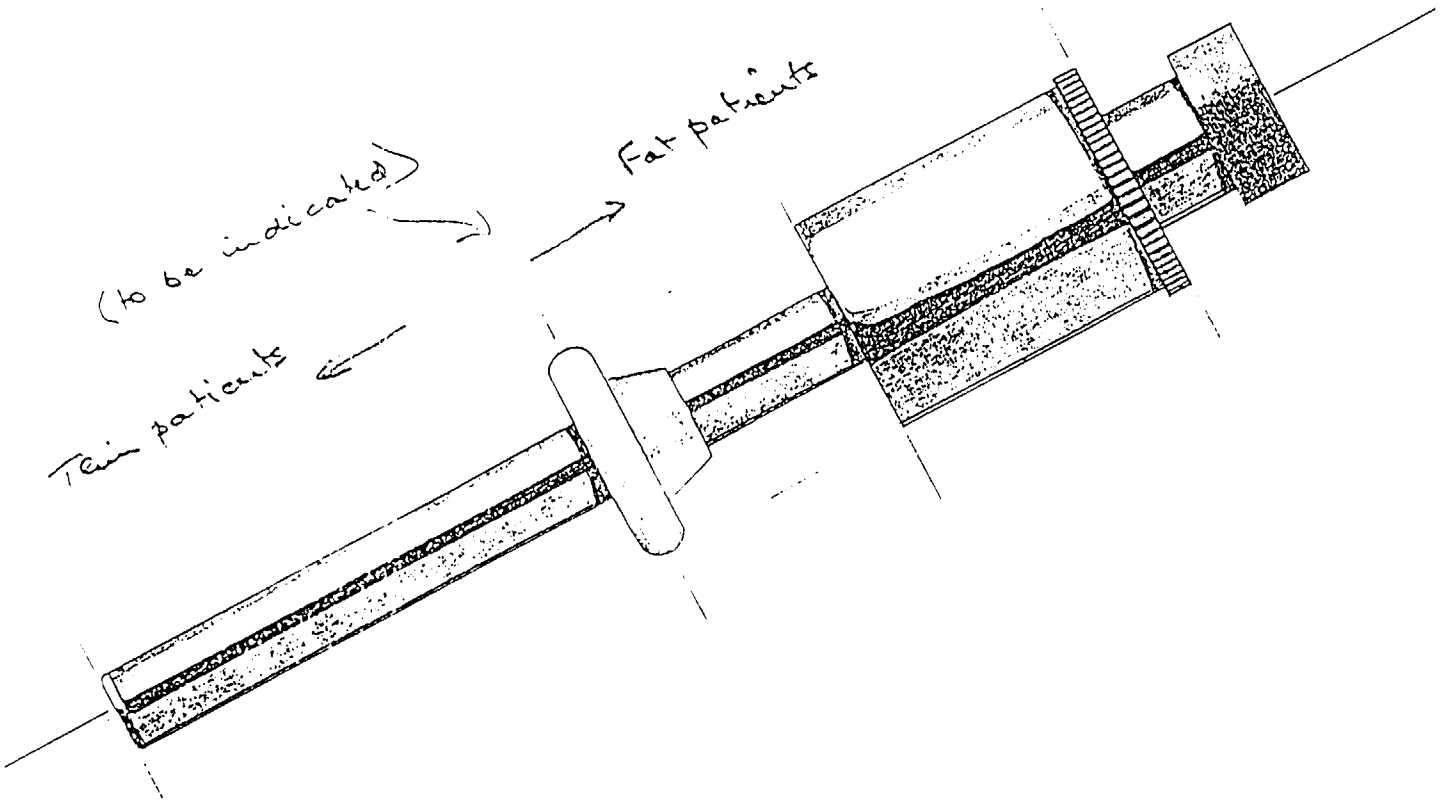


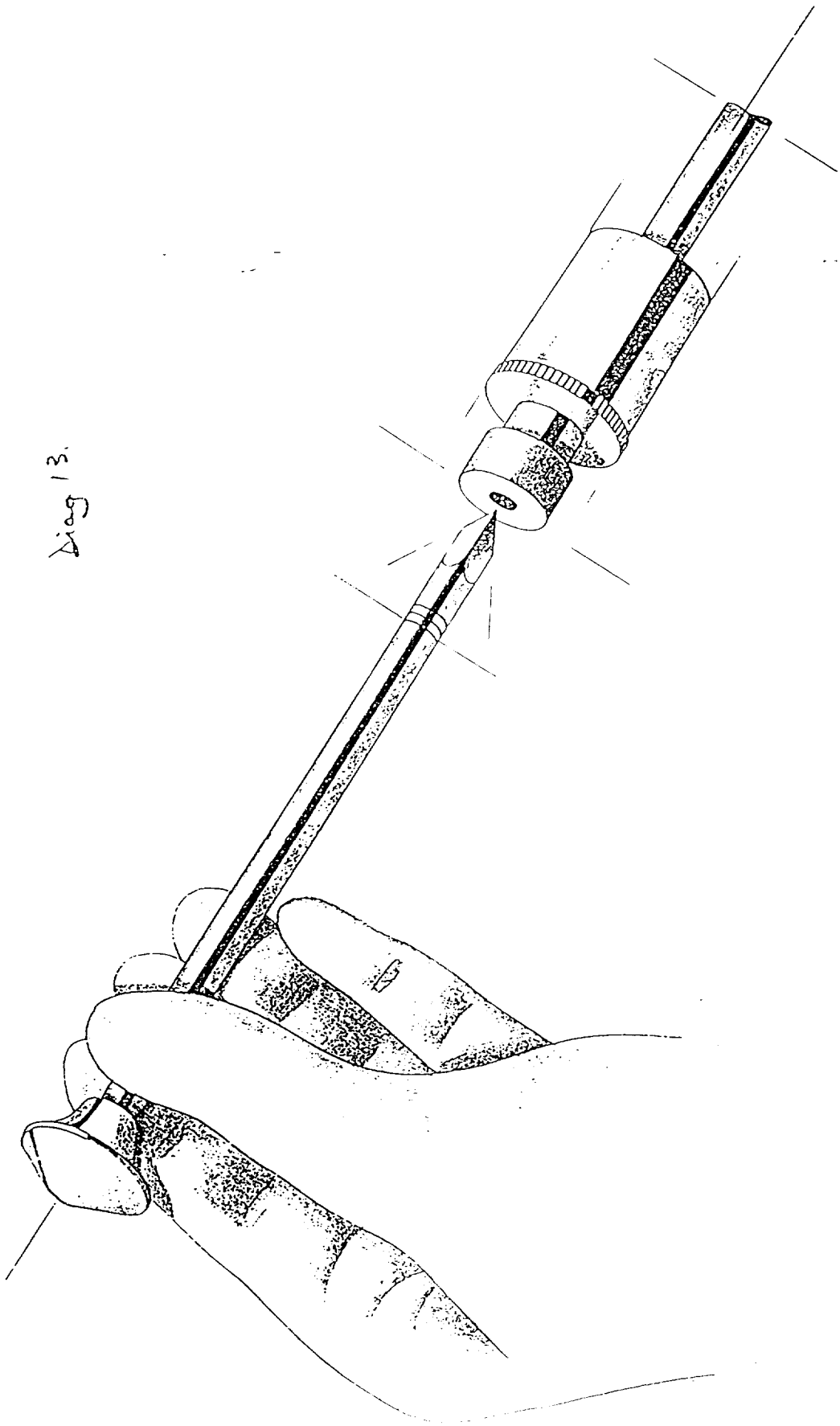
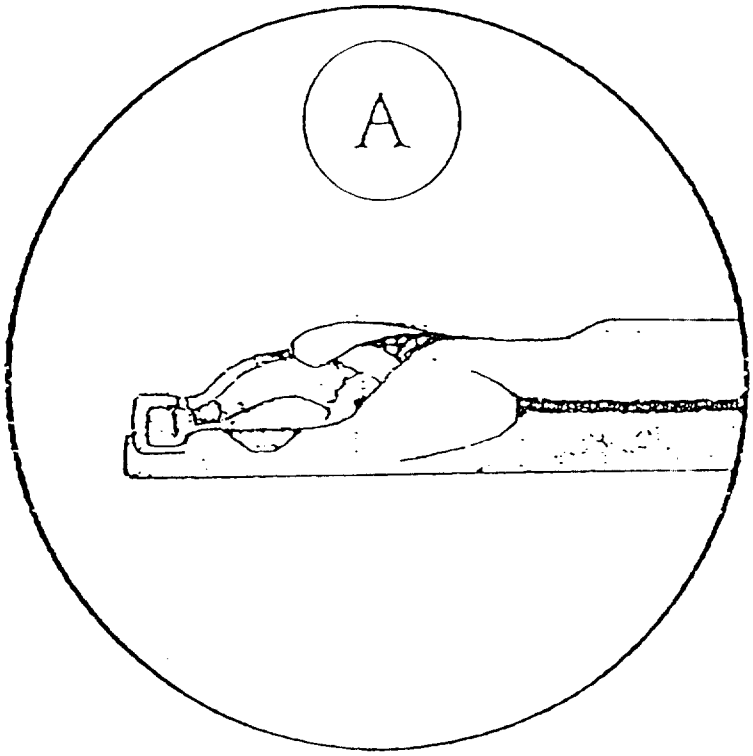
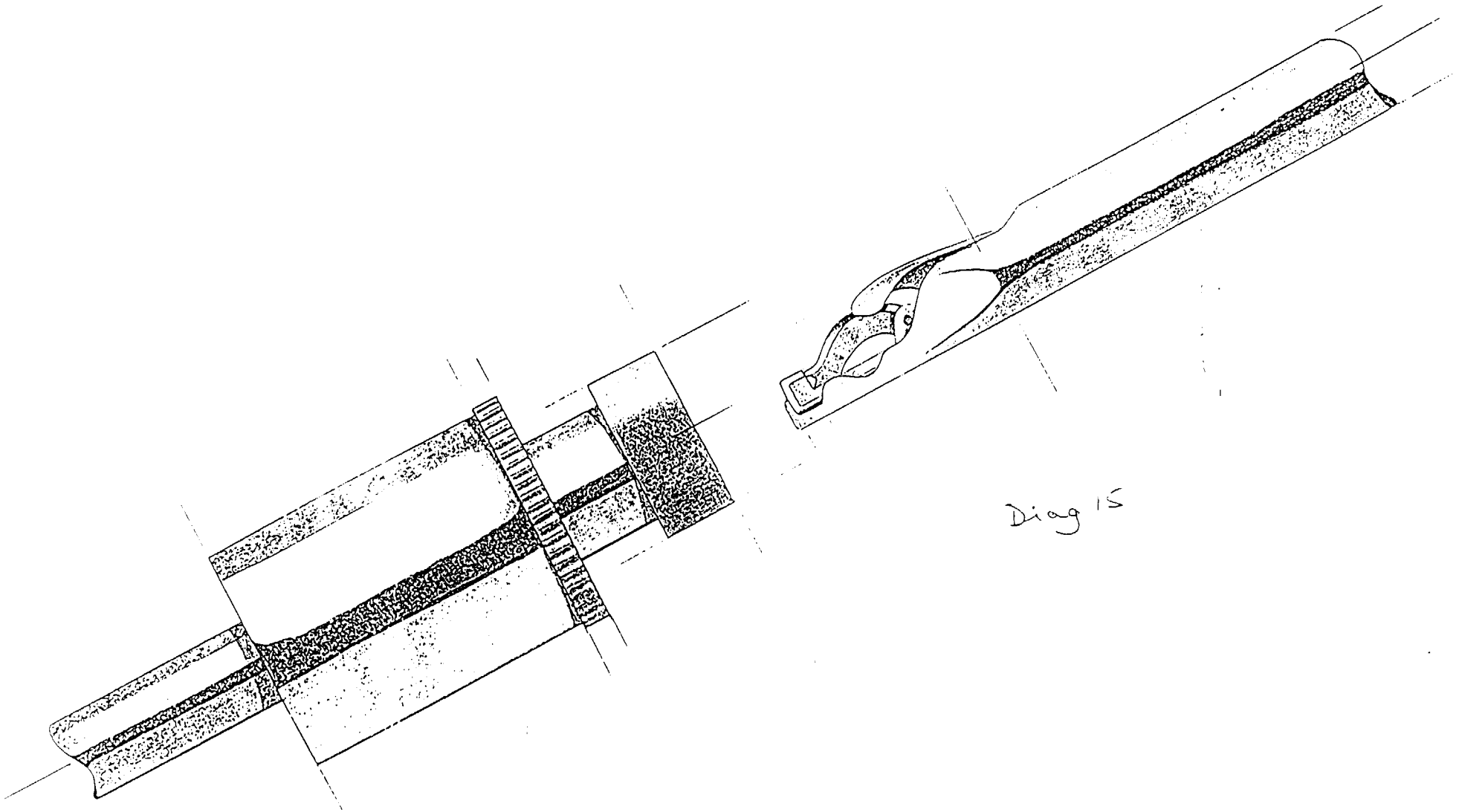


Fig 13.

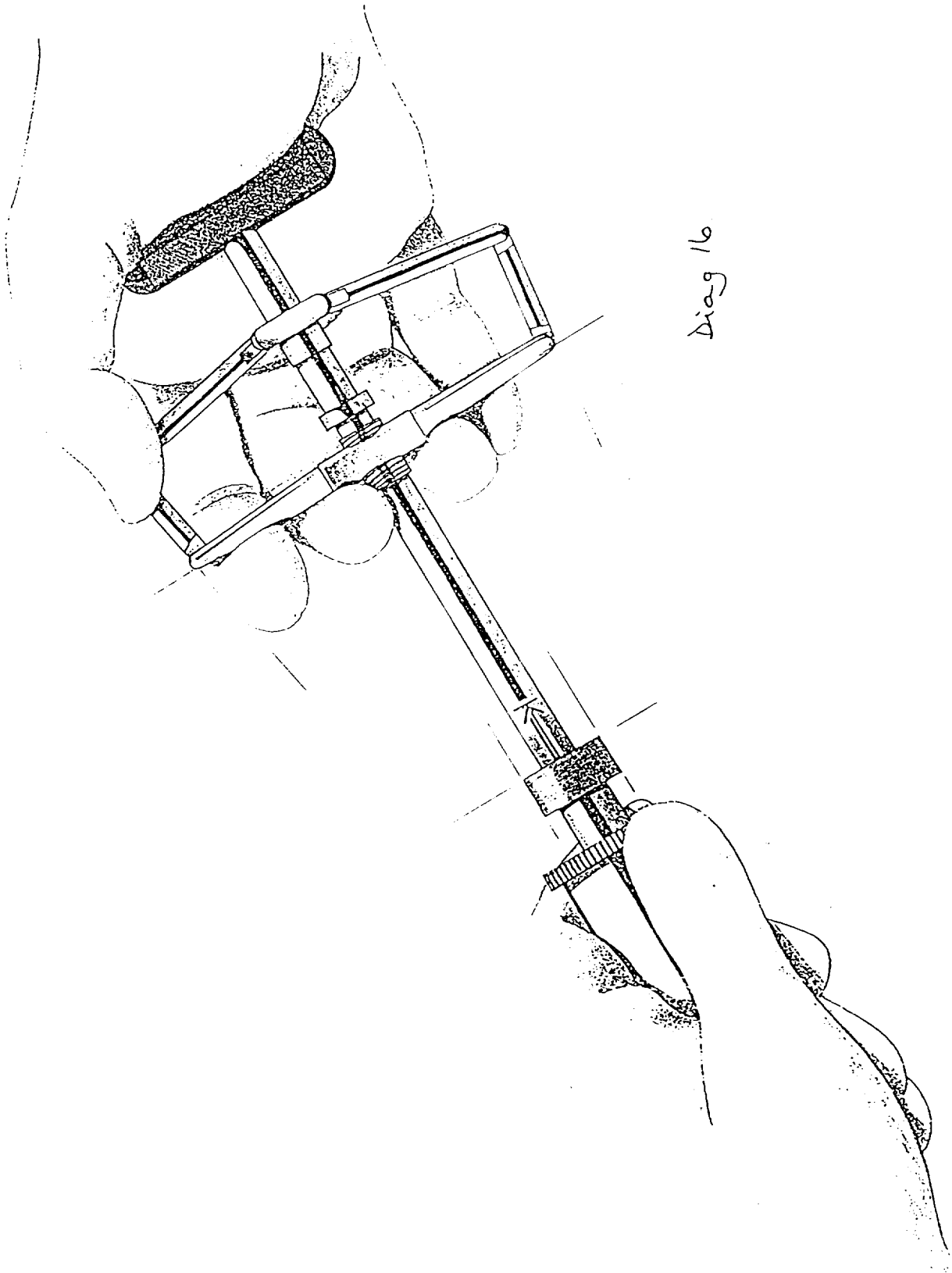
Diag 14

(Sorry about the quality. This will be put right on final publication)



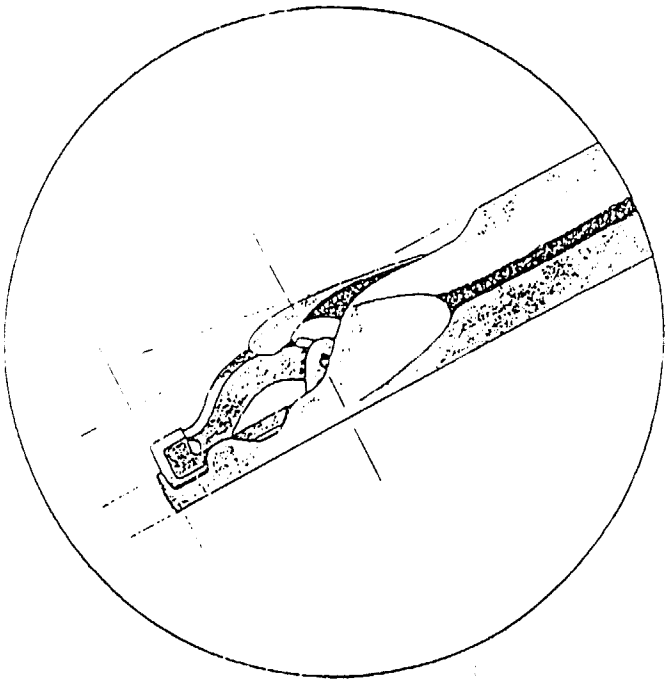


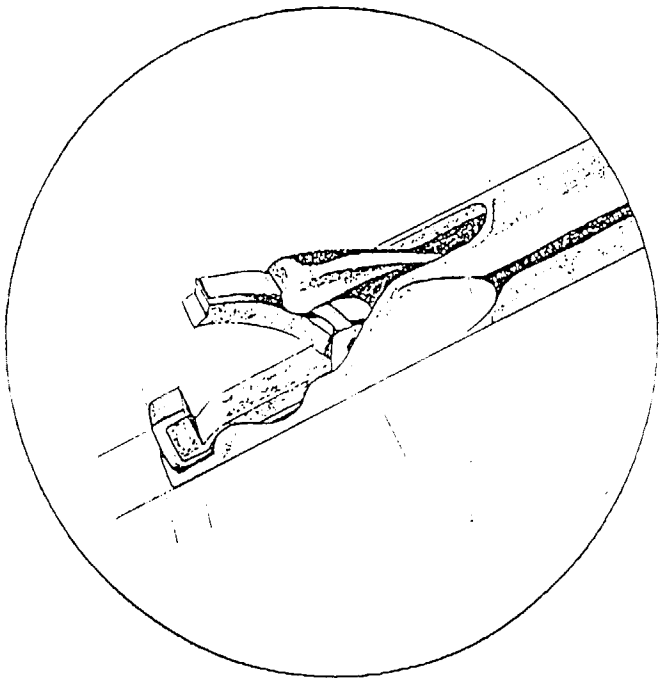
Diag 15



Diag 16

Diag 17





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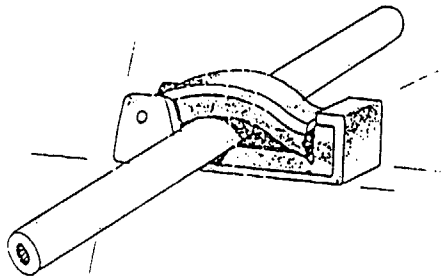
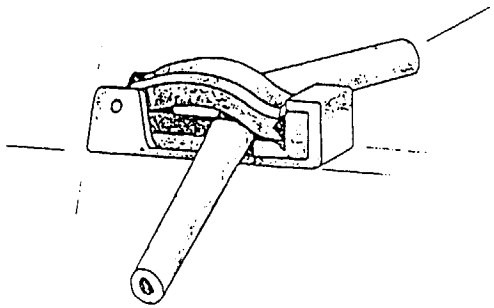
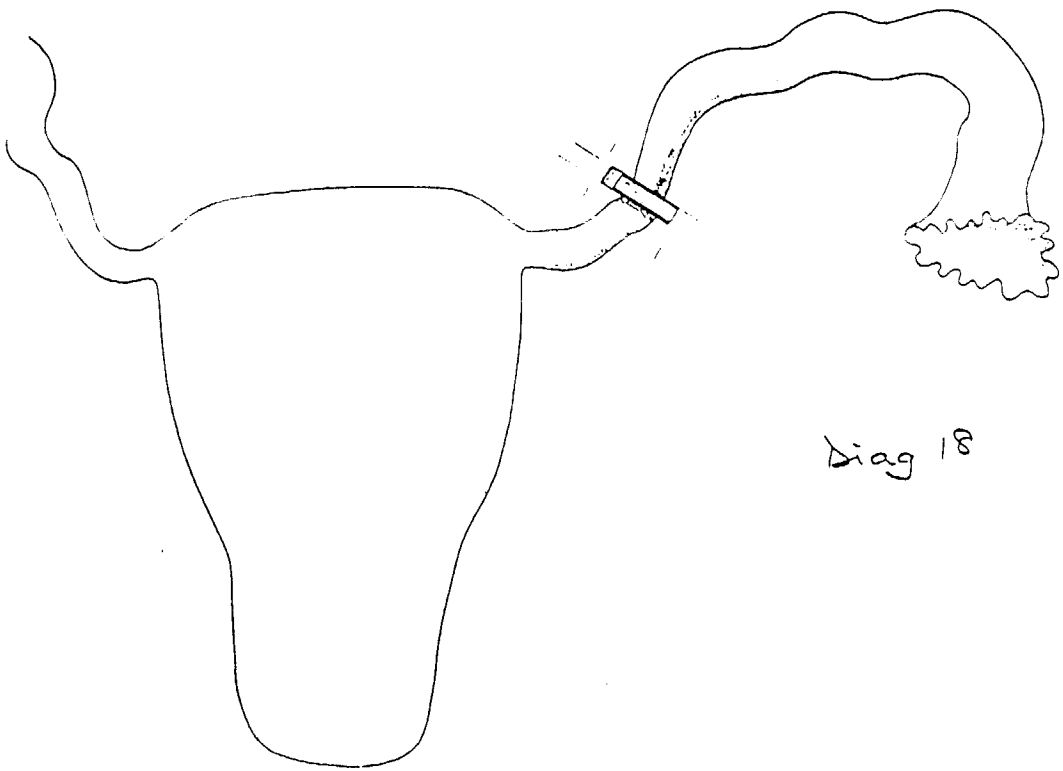
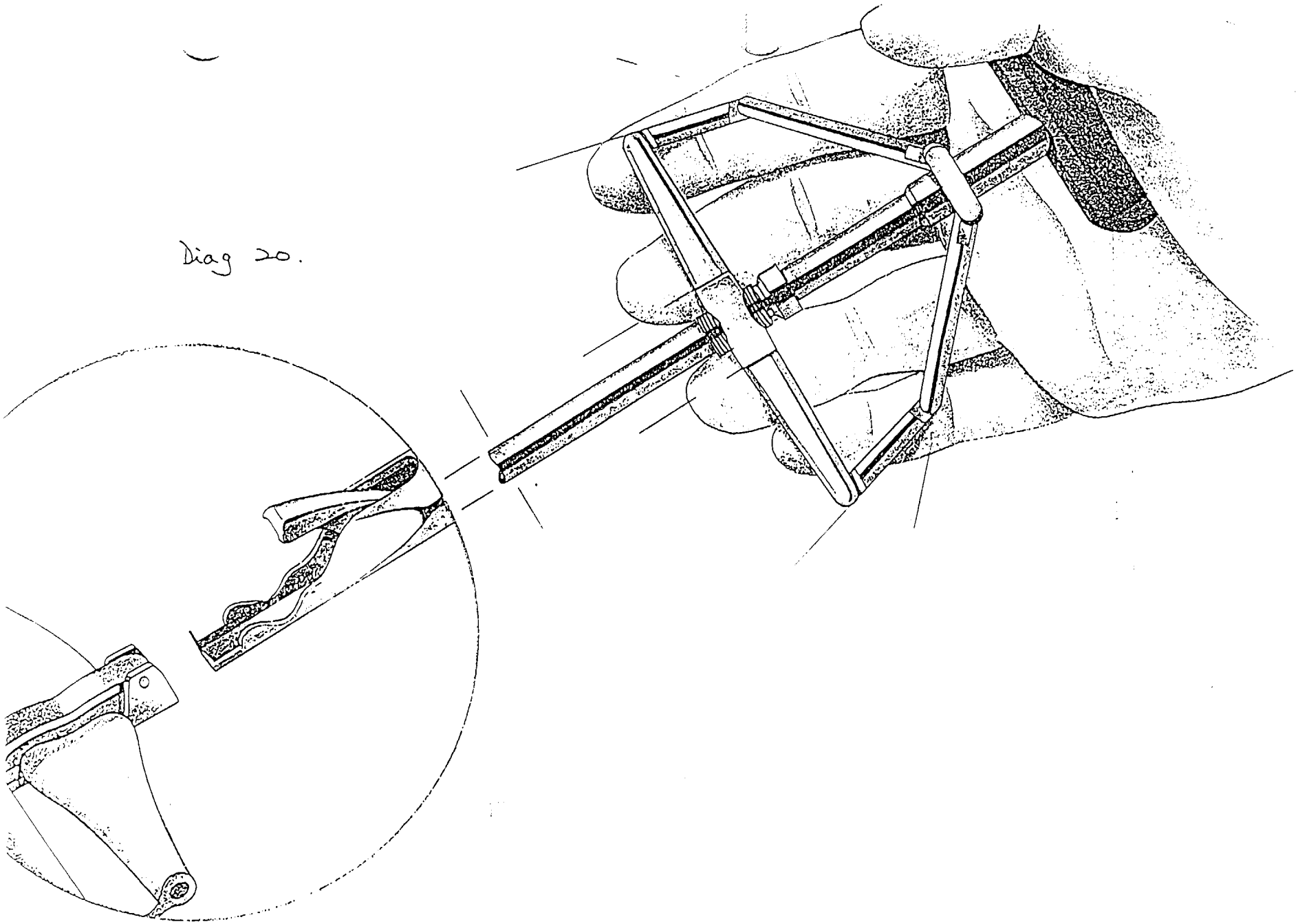






Diag 18

Diag 20.



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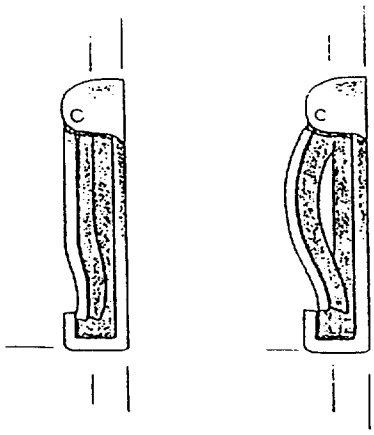
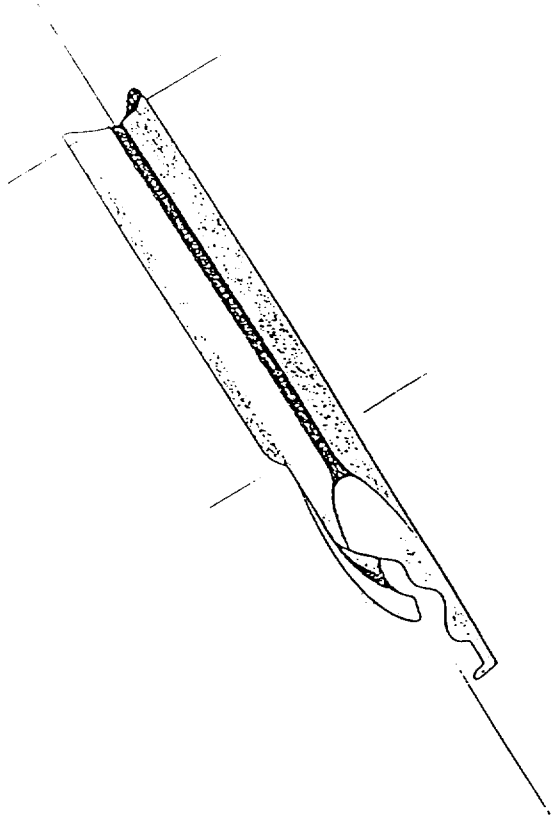
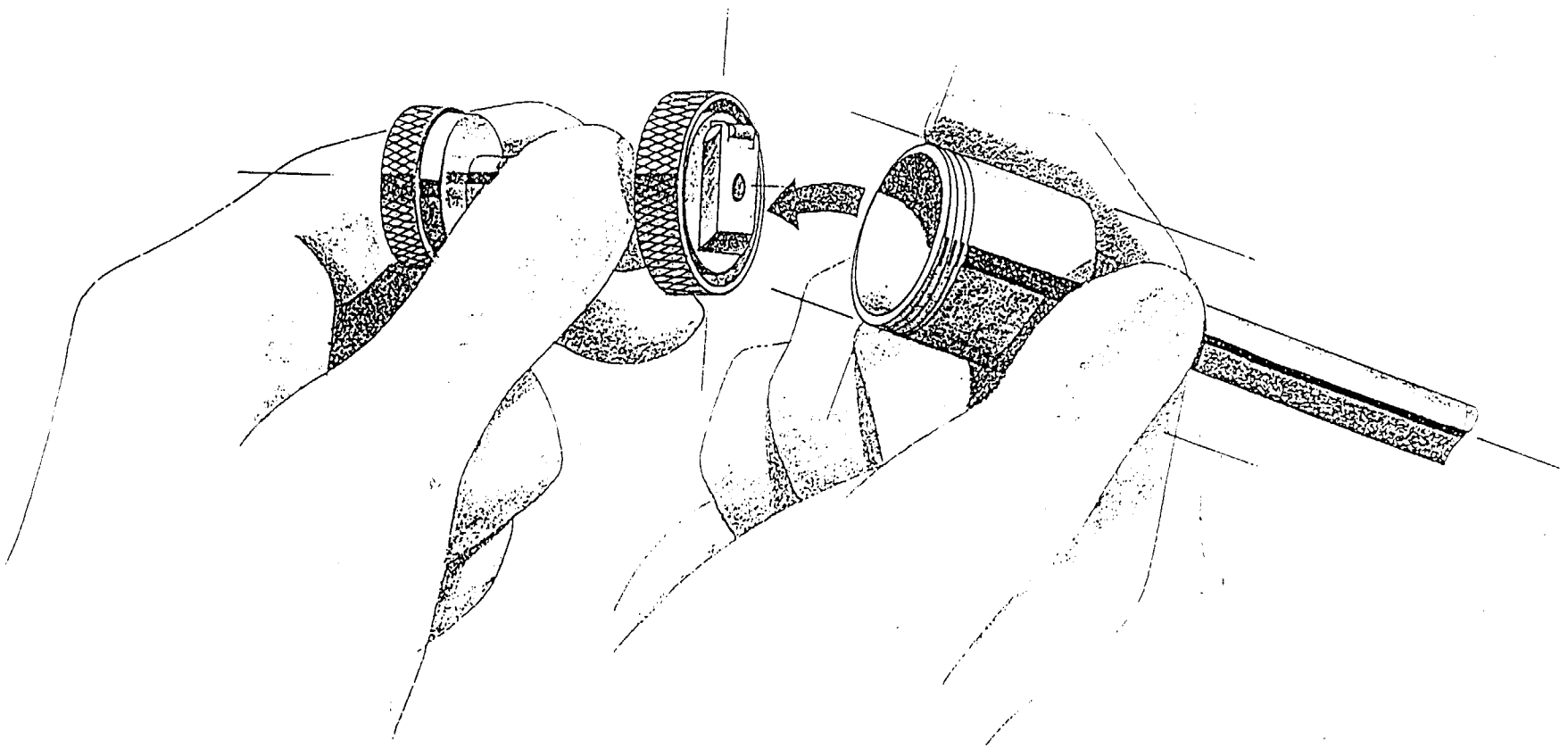
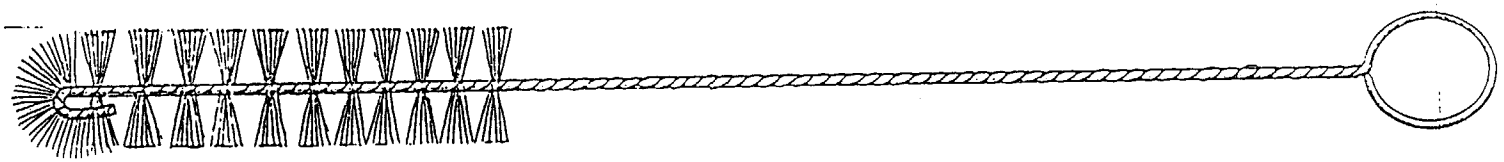
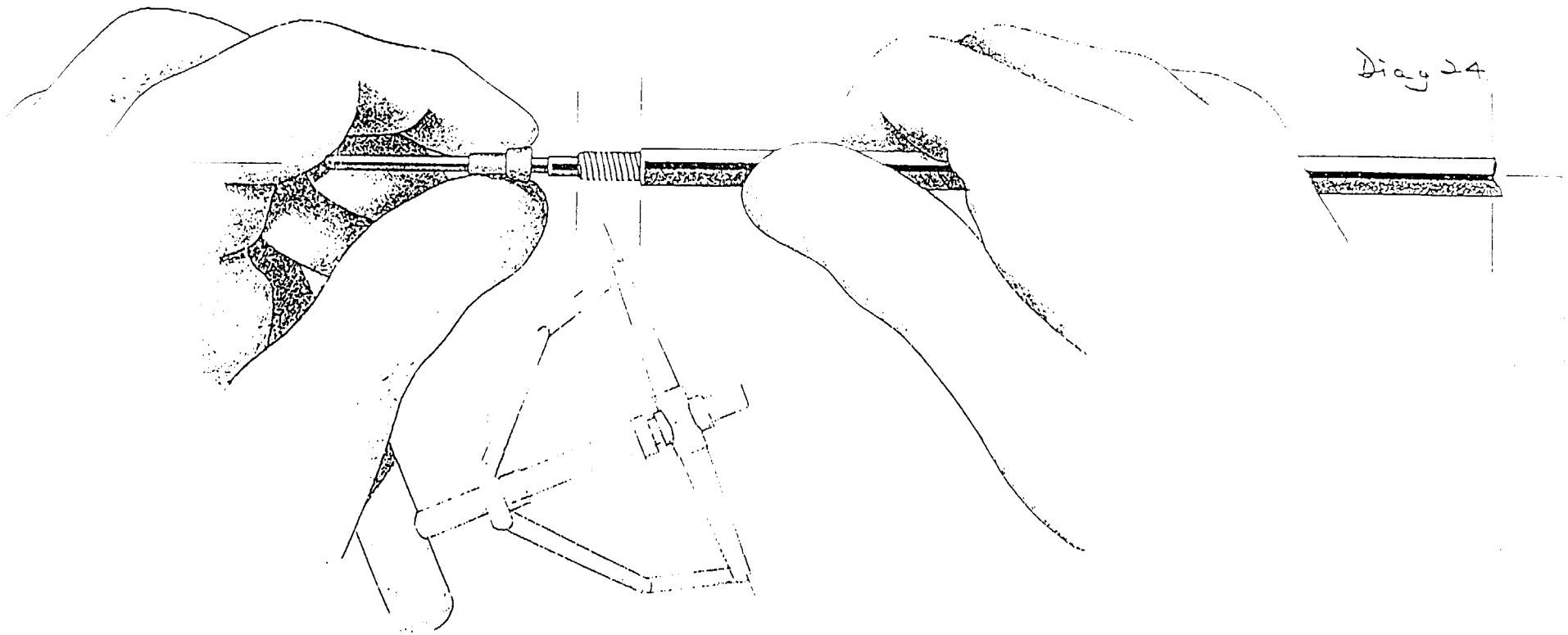




Diag 22 & 26







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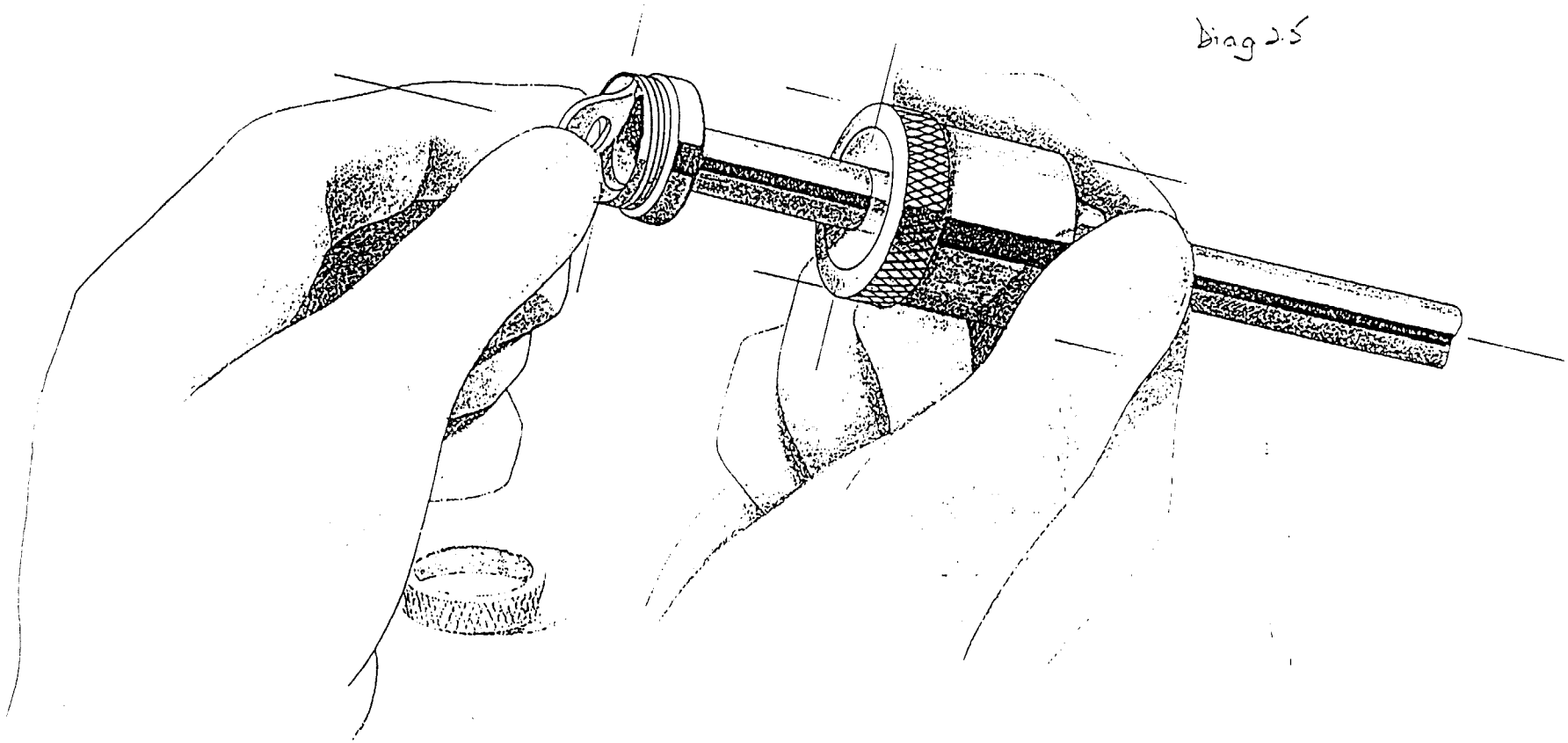
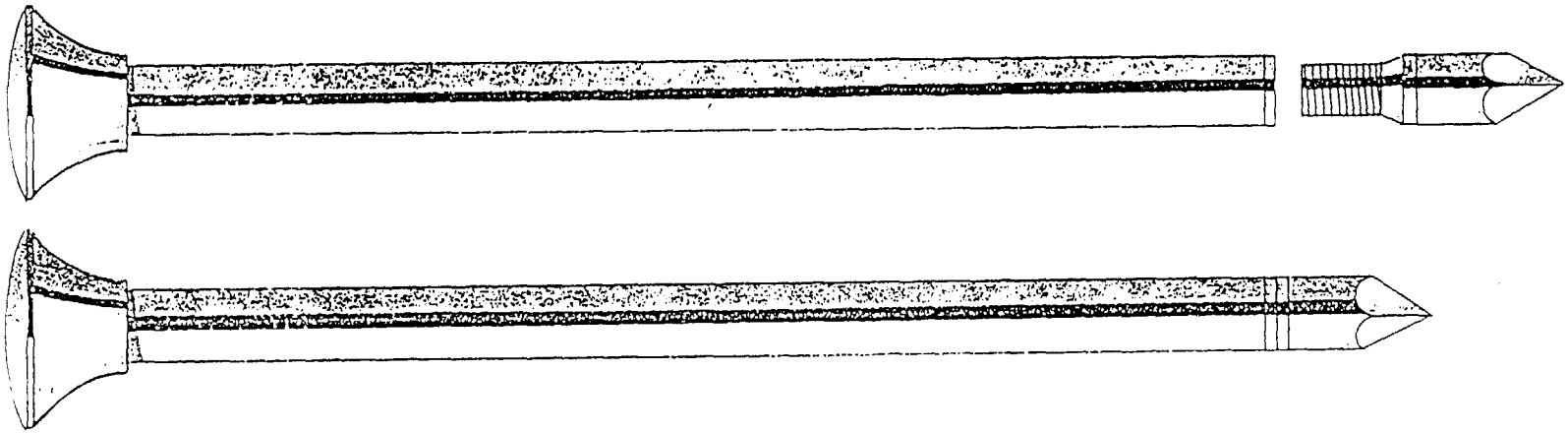


diag 2.5



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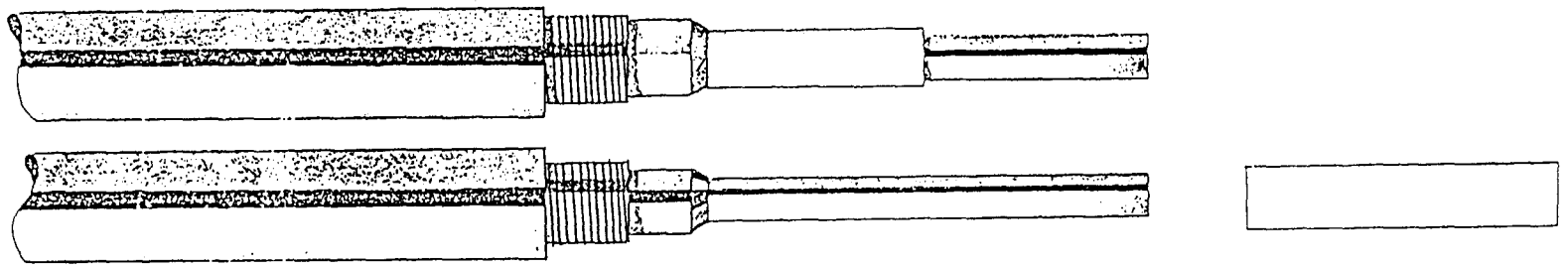

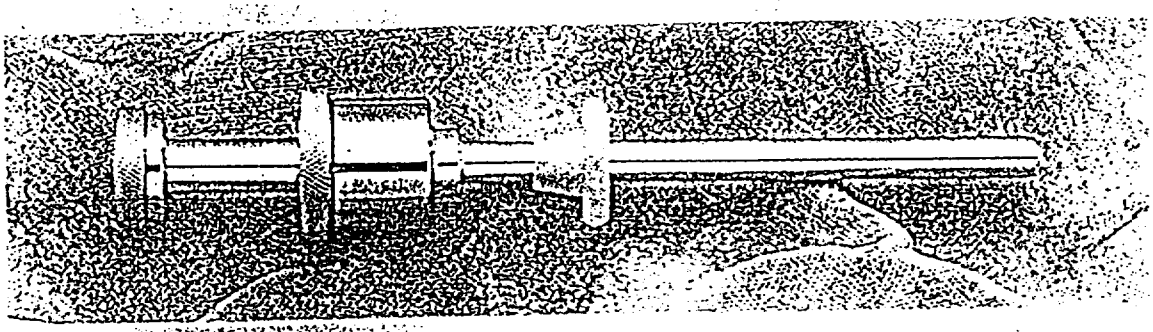

Diag 28.

Appendix III

CAUTION: Federal (USA) law restricts this device to sale, distribution, use by, or on the order of a physician with appropriate training and experience.

FEMCARE

ONE PAIR FILSHIE CLIPS FOR TUBAL OCCLUSION

STERILE

LOT No.
STERILISATION DATE
STERILE UNTIL [date]*

Cook Pharmica Inc
[illegible]

FEMCARE LIMITED
[illegible]

** Shown on reverse.

*6 months from date of sterilization